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Level of compliance with a gluten free diet and nutritional status of adult's patients with coeliac disease

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ELIZABETH SILVA FERREIRA ALVES

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ABSTRACT

Background: A good compliance to gluten free diet is an important part of coeliac disease management, which requires total commitment on the part of patients, as prevents further complications related to the disease. This study aimed to verify the level of compliance with a gluten free diet and the nutritional status of patients with coeliac disease.

Methods: A Coeliac Dietary Adherence Test was assessed in 86 adults' patients with coeliac disease (63 female and 23 male, aged 19-64) who were on a GFD for more than 3 months. Dietary intake using 3-day food diary and BMI were also obtained and analysed.

Results: Seventy-one patients were identified as compliant and 15 as non-compliant. A higher percentage of non-compliant (46.7%) patients committed dietary transgression compared to compliant (22.5%). Percentage of compliant patients (33.8%) who reported did not receive gluten free diet on prescription was lower than non-compliant (40%). All patients had low intake of energy intake, protein, fibre, fibre energy density and high intake of carbohydrate, compared to Dietary Reference Intakes. Vitamin B12 was the only macronutrient according to the nutritional recommendation. High difference was found in fibre energy density between compliance groups (p=0.029). None of non-compliant met the RNI-intake of calcium, folate and fibre. Both compliance groups were classified as overweight. BMI were highly correlated to energy intake (p=0.004), fat (p= p= 0.026) and fibre (p=0.041). It was found presence of symptoms in 82.6% of the all patients.

Conclusion: Despite this study has found high percentage of compliant patients, presence of nutritional deficiency and persistent symptoms were verified amongst those patients. This shows that all facets of the disease, not only gluten avoidance, should be analysed when is addressing about the treatment of celiac disease.

Key words: Celiac Disease, compliant and non-compliant, and Nutritional status.

1. INTRODUCTION

Coeliac disease (CD) is known as an autoimmune response that occurs in the mucosa of small intestinal due to exposure to gluten-containing food, which consequently leads to atrophy of villous, inflammation and malabsorption (Norström *et al.,* 2012). Although, once CD has indicated as an uncommon disorder, new screening researches have demonstrated that CD prevalence has increased and affects 1% of European population. However, many cases of CD continue undiagnosed (Capriles *et al.,* 2009). CD is found in all age, but it has been detected commonly in adults (Lohi *et al.,* 2007). CD pathogenesis ranges from genetic predisposition to environmental exposure, and its clinical presentation is varied. Since, it can result in malnutrition, and as well as, in gastrointestinal symptoms. Undetected cases of CD are characterized by atypical symptoms, which includes few or none gastrointestinal symptoms (Capriles *et al.,* 2009; Mein and Ladabaum, 2004). The only Treatment accepted for CD is a strict gluten free diet (GFD), wherefore, it is natural to assume that after GFD introduction, patients have an recovery of the enteropathy and an improvement of absorptive area, which may lead to an adequate nutrients absorption (Ohlund *et al.,* 2010). Furthermore, it was reported that patients treated effectively with a total GFD, they may obtain an excellent prognostic and likely live a normal life. A poor CD management or non-compliance with a GFD may lead to persistent symptoms, and consequently, to complications such as, malignancy and mortality (Bellini *et al.,* 2011; Freeman *et al.,* 2009). Nevertheless, many studies have investigated compliance with a GFD and shown that compliance with a GFD is not totally unanimous (Fabiani *et al.,* 2000; Rashid *et al.,* 2005; Comino *et al.,* 2012). Compliance with GFD is important for the success of CD management and it depends on Patients, caregivers and experts of CD (Ohlund *et al.,* 2010; Leffler *et al.,* 2007).

2. Literature Review

2.1. Coeliac disease

Coeliac disease is a chronic condition that is described as an inflammatory enteropathy response to gluten ingestion in individuals who are genetically susceptible (Niewinski, 2008; Vincentini *et al.,* 2011). Gluten is named as prolamin that is a protein fraction present in wheat, barley, rye and oats, in country like Australia. Gluten is named as prolamin that is a protein fraction present in wheat, barley, rye and oats, in country like Australia. The damage of small bowel mucosa is the major characteristic of CD (Planas *et al.,* 2011). This impairment initiates first in the duodenum and later advances to the ileum. The impairment of small bowel mucosa occurs followed by progressive levels of villus damage and inflammation, which results in crypt hyperplasia induction (Eid *et al.,* 2013). Villus loss and crypts hypertrophy leads to a chronic excess of fluids including the epithelial infiltration of T cells in the lumen of small bowel (Ciclitira *et al.,* 2005; Eid *et al.,* 2013; Du Pre *et al.,* 2015), and as well as, to a poor absorption of essential vitamins and minerals, such as, iron, vitamin B12, calcium, folic acid, (Edi *et al.,* 2013). Clinical picture of CD ranges from asymptomatic to a typical presentation, and it relies on several factors including age, onset, duration and severity of the disease (Reilly and Green, 2012; Mazzone *et al.,* 2011; Nachman *et al.,* 2009). The symptoms when manifest consist of abdominal pain, diarrhoea, weight loss, fatigue and nausea (Sainsbury and Mullan, 2011). Therefore, CD is highly associated to anaemia, osteoporosis and neuropathy (Nachman *et al.,* 2009; Addolorato *et al.,* 2004) and when untreated can progressively causing infertility, osteopenia, venous thromboembolism, intestinal and bowel cancers, secondary hyperparathyroidism and other autoimmune complications (Eid *et al.,* 2013; Krupa-Kozak, 2014; Norström *et al.,* 2012; Ludvigsson *et al.,* 2011). Asymptomatic CD includes a small intestine damaged, a serology positive and no symptoms (Mazzone *et al.,* 2011; Nachman *et al.,* 2009; Addolorato *et al.,* 2004).

Coeliac disease was once seen as childhood disease but it has been shown to affect young and elderly similarly (BIngley, 2004; Godfrey *et al.,* 2010). It is

a worldwide disease affecting almost 1% of universal population with an occurrence of 6 per 100 children and 1 per 100 adults (Susanna and Prabhasankar, 2015). This has been demonstrated to be similar among adults population in United Kingdom, affecting approximately 1 in each 87 adults. Additionally, in Europe, cases of CD have increase significantly and it have also related to recent increase in mortality (Häuser *et al.,* 2010; Leffler *et al.,* 2008; Godfrey *et al.,* 2010). Although, CD is most common in Caucasians individuals, it is believed to be uncommon in East Asia, as well as, in central Africa. Furthermore, The increase prevalence of CD seems to be due to an extensive serological testing, and as well as, the highest level of recognition and awareness (Krupa-Kozak, 2014). Curiously, this increase in prevalence of CD is higher among women than men, in which 2 in each 8 females have CD in contrast to 1 in each 8 male. It is believed that this increase is associated to evidence that CD is mostly detected in men when they are at an older age (Gujral *et al.,* 2012). When CD is suspected biopsy of small bowel is the standard method used to the final diagnosis, along with the biopsy of the duodenal. Recent serologic tests, such as, antibody testing, have been also included, and it has also shown to be an effective and highly sensitive method (Frulio *et al.,* 2015; Godfrey *et al.,* 2010). Antibody testing includes endomysial antibodies and transglutaminase. However, the first indication of CD presence may delay to appear (Norström *et al.,* 2012). Currently, a rigorous gluten free diet (GFD) has proved to be the key treatment for CD. GFD is important and beneficial in the recovery of the small bowel function and structure (Niewinski, 2008).

2.2. **Gluten free diet (GFD)**

Avoidance of natural or processed foods containing gluten is undoubtedly the best description of a gluten free diet (Rajpoot and Makharia, 2013), since GFD is the only acceptable therapeutic treatment for patients with CD and it is for all life (Green *et al.,* 2015; Bellini *et al.,* 2011). This diet seems to improve clinical aspect of the disease by ameliorating clinical and laboratory parameters, attenuating symptoms, and probably avoiding the risk of long-term complications (Sainsbury *et al.,* 2013). Many important studies have

shown evidence that supports the positive effects of treatment with GFD in CD patients who have typical characteristics of CD (Nachman *et al.,* 2009). A strict GFD has shown to normalize the small bowel mucosa, which is very important to a better functionality of gastrointestinal, including improvement of nutrients absorption, which means a better life for CKD patients (Frulio *et al.,* 2015; Akobeng and Thomas, 2008). However, a little recovery in the intestinal mucosa may occur in months or years depending on the patients and the disease state (Collin *et al.,* 2004). In a prospective study with 57 CD adults' patients and 83 control participants was shown the effects of GFD introduction in duodenal morphology. The findings demonstrated that after 4 years of GFD there was an improvement in villous area, as well as, a reduction of crypt measurement. However, this changes in morphometric indices was not associated with dietary compliance with a GFD but this was highly correlated to the anti-endomysial IgA antibody disappearance (Cummins *et al.,* 2011). Additionally, a study in patients with urticarial and with celiac disease has reported that gluten free diet reduces clinical symptoms related to skin and intestine. Since the increase of mucosa permeability followed by passage of antigens may lead to lesions of urticarial. Therefore, recovery of the mucosa integrity with a strict GFD seems to improve skin symptomatology and then urticarial (Abenavoli *et al.,* 2006). GFD has also shown to increase bone mass density or to maintain it stable in patients who follow GFD for at least 1 year. The results showed an improvement of bone mass density at the lumbar spine level in 52% of CD patients, at the femoral neck (46%), as well as, at the trochanter level (68%). Furthermore, as it was a 5-year follow-up study, the authors considered the outcomes as a positive response of CD patients to GFD (Kemppainen *et al.,* 1999). Similarly, other studies have reported that strict GFD leads to a normal content of bone mineral and to a normal bone height, and as consequent, improvement of their body composition (Bardella *et al.,* 2000). Other strong indication of GFD beneficial preventive effects in CD is related to malignancy. Study has shown that rates of malignancy tend to be higher among Individuals with untreated celiac disease compared to general population. This study has also shown when a patient is on a gluten free diet up to 5 years, their risk to lymphoma, and carcinoma of small bowel are relatively equal to general population (Haines *et al.,* 2008). Concerning to

association between CD and other comorbidities, there is no significant studies showing the benefits of GFD treatment in patients with both diseases (Hill *et al.,* 2005). Although, it has shown GFD effectiveness and benefits, studies have revealed that a significant percentage of patients do not respond positively to GFD, in terms of improvement of symptoms. A study has shown that almost 30% of individuals treated with GFD are not benefited with improvement of symptoms that are associated to CD. This non-responsive coeliac disease is characterized by the continue presence of some symptoms, such as, abdominal pain, lethargy and diarrhoea in patients following GFD (Dewar *et al.,* 2012). This was also reported in other study with less percentage of individuals, 5-10%, and which also reported presence of persistent villous atrophy and continued CD symptoms (Häuser *et al.,* 2010). Lack of adherence to GFD may be related to these findings. However, studies have shown that even a small quantity of daily gluten intake can cause changes in the small bowel mucosa biopsy. The exact quantity of gluten which CD individuals are allowed to consume and tolerate regularly, without any harmful effects still was not determined (Akobeng and Thomas, 2008). This Disagreement surrounding the classification of a GFD is due to lack of techniques for identifying gluten, as well as, lack of consistent scientific findings to determine the threshold of minimal gluten intake, which do not bring negative effects in the intestinal mucosa. GFD management depends on incessant collaboration, commitment and awareness of the patients, families and specialists, mainly, dieticians (Hill *et al.,* 2005; Comino *et al.,* 2012).

2.3. **Dietary adequacy and celiac disease**

CD is directly related to malnutrition around world, which is consequential of malabsorption. Earlier evidence has reported that over than 20% of CD individuals suffer from some nutritional deficiencies, which range from severe to mild deficiencies. These include deficiency of energy and protein, as well as, fibre and micronutrients deficiencies (vitamins and minerals) (Goyens *et al.,* 1985; Wierdsma *et al.,* 2013). Other common complication that is secondary to nutrition is lactose intolerance. This happens by low production of lactose caused by damage to the villi (Niewinski *et al.,* 2008). Furthermore,

amongst the nutrients deficiencies, folate, iron and calcium is commonly related among CD patients, since the absorption of these nutrients occurs in the proximal small bowel (Saturni *et al.,* 2010). Iron deficiency has been reported in 12% to 69% of CD Individuals (Halfdanarson *et al.,* 2007). Vitamin B12 deficiency has been shown to be significantly lower in untreated CD patients due to a reduction in area of absorption caused by villous atrophy (Halter *et al.,* 2002). Malabsortion of calcium, phosphorus and vitamin D are caused by pathology and mechanism of the disease (Rujner *et al.,* 2004). Although, there is no many evidence related to the effects of macronutrients malnutrition in adults, studies has been demonstrated that in children can occur growth delay (Haines et al., 2008, Mearin *et al.,* 2005). These nutritional deficiencies can cause secondary complications (West, 2004). For instance, iron may cause anaemia, fatigue and cognitive damage (Harper *et al.,* 2007). Folate may also be involved in cases of anaemia and related to high level of homocysteine, which may result in thrombosis, osteoporosis and recurrent abortion (Haines *et al.,* 2008; Yazynina *et al.,* 2008; Bergamaschi *et al.,* 2008). Similarly, calcium and vitamin D are also linked to osteomalacia and osteoporosis (Rujner *et al.,* 2004). Vitamin E deficiency has been associated to neurological disease and selenium to thyroid function in untreated patients with CD. Therefore, the severity of nutritional disorders depends on the degree of malabsorption and intestinal mucosal damage, and as well as, the period of time that the disease remained active and without being diagnosed (Haines *et al.,* 2008). Studies have shown that many of these nutritional deficiencies can be treated followed by a strict GFD. For instance, studies have shown that after introduction of GFD there was an increase in calcium absorption in patients with CD (Capriles *et al.,* 2009). GFD was also shown to improve iron deficiency, consequently, restoring growth problems in CD children (See and Murray, 2006). However, others have reported that GFD is not a guarantee of an appropriate nutritional intake, and that some of these deficiencies appear after therapy with GFD for more than 7 years (Saturni *et al.,* 2010). Additionally, studies that examined dietary history of adults with CD reported that their diet is nutritionally adequate only the early years of treatment (Hallert *et al.,* 2002). Other researches have explored the nutritional composition of processed GFPs and they showed that the level of lipids,

carbohydrate and salt are high in patients with CD (Saturni *et al.,* 2010). In a similar study, was also shown an increase in fat and protein intake, and as well as, a decrease in fibre and minerals intakes, such as, iron and calcium (Hopman *et al.,* 2006). Therefore, malabsorption effects can be severe in untreated or undiagnosed individuals and mainly in patients with a previous poor nutritional status (Rajpoot and Makharia, 2013).

2.4. **Gluten free products (GFPs)**

Gluten is the most important protein of structure formation in flour, and thus it plays an important role in baked products. Since, gluten gives the elastic appearances to the dough, as well as, is responsible for the crumb structure improvement and for the features of several baked products. Gluten withdrawal means a big problem and challenge for the bakers (Gallagher *et al.,* 2004; Rajpoot and Makharia, 2013). Developing gluten free products with both great quality and nutritional value for the CD patients remains a major concern for the food industry. Many GFPs offered by the market still have some quality problems including poor sensory quality and shelf life compared with wheat products (Phimolsiripol *et al.,* 2012; Laureati *et al.,* 2012). For instance, typical gluten free bread seems to be denser when compared to typical non-gluten free bread (Haner, 2005). In most cases, the introduction of GFD causes confusion and concerns, regarding to gluten free foods that are allowed and included or which are not. Gluten free foods are distinguished in two types: foods naturally free of gluten and food produced without gluten by a purification process (Penagini *et al.,* 2013). Naturally GFPs includes fruits and vegetables (frozen, canned or fresh); vegetable oils, beans, corn, rice, seeds, some different grains and pseudo-cereals (amaranth, quinoa, Buckwheat), fish, meats, eggs and dairy products. In the UK, it is perhaps allowed the use of wheat starch, which was extracted the gluten (Yazynina *et al.*, 2008). Processed gluten-containing food not included in GFD are breads, pasta, pizzas, cereals, snacks, biscuits, sauces, soups, marinades, seasonings, soy sauce, some desserts, packaged flavoured rice, and processed cheeses (Niewinski *et al.,* 2008; Penagini *et al.,* 2013). Furthermore, it is also included medications that contain gluten (Gallagher *et*

al., 2004). Gluten free food is an economic burden for CD individuals, despite little study addressing this topic. However, it has been demonstrated that the food cost for patients with CD is clearly greater than is for general population (Long *et al.,* 2010; Whitaker *et al.,* 2009). Furthermore, CD women require more health care compared to non-CD women (Norström *et al.,* 2012). Although, GFPs require greater expense compared to those containing gluten, it seems recently eating GFPs has become less complicated by the increase of the GPs available to be purchased by mail, in supermarkets or in pharmacies (Kinsey *et al.,* 2008). In addition, patients can buy a variety of gluten free products, including flours and baking mixes, and also many gluten free cookbooks have been very useful providing a number of recipes and advices for gluten free costumers. This availability provides a greater food choice for CD patients and an increase in the variety of the diet, which enables patients feel normal when they are with relatives (Niewinski *et al.,* 2008). However, a complete elimination of gluten cannot be achieved, if not impossible, since gluten contamination can occur in GFPs, which makes very difficult to avoid gluten totally (Akobeng and Thomas, 2008). Cross contamination can occur from the harvest to storage, and as well as during transport and manufacturing. For example, oats that despite being considered a food without gluten, oat marketed may suffer contamination with grains containing gluten and this can also occur with other products free of gluten (Thompson *et al.,* 2003). Thompson et al., (2010) in their study with 22 types of grains, seeds and flours considered inherently gluten free and that were not labelled as gluten free, found that 32% of them could not be considered as gluten free product as the level of gluten content were over than 20ppm. It is crucial that CD patients ensure through food labels or food companies that consumed product are free from gluten (Niewinski *et al.,* 2008). Despite small gluten content in GFPs, in which may be harmless for many patients, this can lead to serious effects on individual with CD (Collin *et al.,* 2004; Catassi *et al.,* 2007). Authorities of the food regulating organization recommend that for a GFP be considered as free from gluten, the level of gluten content should be less than 20 mg/Kg, and denominated as very low gluten content whether the gluten content level is between 20 mg/Kg-100mg/Kg (Food Standards Agency, 2012). Therefore, GFPs must be clearly labelled and CD patients

have to be well informed or educated in order to interpret them without mistakes. This helps CD patients choose the best GFPs (Penagini *et al.,* 2013).

2.5. **Compliance with a gluten free diet**

Compliance with a gluten free diet can be assessed using laboratory, histological and clinical information, and dietary intake (Capristo *et al.,* 2000; Cummins *et al.,* 2011). Many patients consider adherence to GFD as a challenge and difficult to adhere to because GFD can be very restrictive, and also because a little amount of gluten can stimulate serious results on clinical and histological parameters (Mayer *et al.,* 1991). Consequently the failure on following their dietary self-management has demonstrated to affects not only the physical but also the psychological of those patients (Rose and Howard, 2014). The adherence to a GFD seems to vary from poor to satisfactory (Butterworth *et al.,* 2004). In children, compliance with a GFD seems to be less affected, as their parents are the responsible for their feeding. In adolescents and adults, it is more complicate, since they tend to give up easily of their dietary management (Errichiello *et al.,* 2010). Among elderly people, the introduction of GFD may not be well accepted, as it requires a new dietary practise, which they may find difficult to comply, as it is necessary to break olds habits. In some case, this non-compliance by this population is cause by little evidence of clinical improvement (Vilppula *et al.,* 2011). Compliance with a GFD requires a significant self-determination on the part of each individual with CD. A recent study shown that the compliance is 69.4% (Araujo and Araujo, 2010) and may range from 45 to 80% (Ciclitira *et al.,* 2005; Hill *et al.,* 2005). The compliance among young people is of 52% to 81% in Europe. This variation in compliance, seems to depend on their believes, importance or reasons related to GFD (Hopman *et al.,* 2006). Importantly, compliance with a GFD has reported to be associated with the recovery of medical conditions, the improvement of nutritional status (Nachman *et al.,* 2009; Capristo *et al.,* 2000; Samasca *et al.,* 2014), and as well as, with decreased of gastrointestinal malignancies (Vilppula *et al.,* 2011), the decreased of symptoms and risk of complications (Sainsbury *et al.,* 2013),

and a guarantee of a better quality of life (Bellini *et al.,* 2011; Nachman *et al.,* 2010). Therefore, Following and maintaining a strict GFD is extremely important for CD population (Sainsbury *et al.,* 2013; Lee and Newman, 2003). It is clear that a lack of compliance can be the major threat for the disease remission. Many factors have been related to non-compliance by the CD patients. This includes cost of GFPs and limited availability of gluten free alternatives (Vilppula *et al.,* 2011; Hall *et al.,* 2009), lack of labelling information and education on the part of patients, family and some stores workers (Biagi *et al.,* 2009); confusion, embarrassment, stress and anxiety (Rose and Howard, 2014); and food contamination (Rajpoot and Makharia, 2013). Thus, understand the factors that are related to a best adherence and obedience to GFD is required in order to improve the resources and develop new strategies to support CD patients (Leffler *et al.,* 2007). Considering that GFD is essential for the control of the CD and health of the patient, and that there are few related studies, it was decided to realize this study (Sainsbury *et al.,* 2013; Leffler *et al.,* 2008).

2.6. **AIMS**

This study aims to verify the level of compliance to a gluten free diet and the nutritional status of patients with coeliac disease. For this purpose, it was measured BMI, dietary intake, and applied a questionnaire related to GFD compliance to NHS celiac patients.

3. METHODS

3.1. Design

This study is a cross sectional study with qualitative and quantitative approach, since this study describes the characteristics of CD population, such as compliance, nutritional status and dietary intake, and thus shows the important aspects related to the objective of this research.

3.2. Sample

Participants of this study came from a PhD study, which is still in progress. It was contacted 1000 CD patients of different ethnicity profile, both gender and who are in database of Leicester General Hospital NHS Trust.

Inclusion and exclusion criteria

All participants were patients with coeliac disease aged over 18, were living in Leicestershire area and were following GFD for at least 3 months. It was also included patients who gave their consent and were able to fill the forms.

3.3. Materials

Demographic Measures

From the hospital database was obtained demographic information including age, gender, ethnicity and CD diagnosis.

Level of compliance

Compliance with a GFD was measured according to Butterworth *et al.,* (2004), and it was complemented using a short questionnaire obtained from a similar study by Leffler *et al.,* (2009) (see Appendix 01). Where was evaluated adherence to GFD using a five point Liker scale, which varied from highly compliant to “not following a gluten free diet at this moment”. Patients who scored from 0 to 16 were considered as compliant and those scored from 17 to 35 as non-compliant. Then a nutritionist who was expert in CD evaluated the patients for GFD adherence.

Three-day food diary

All participants filled a short diary questionnaire of 3 pages with instructions explaining how to use and measure portion sizes (see Appendix 02).

Diet plan 6

It was used the nutrition analysis software package 6 in order to analyse the food diaries (Shepherd and Gibson, 2013). The entire software data sources were used. However, in case of not existence of a GFP on the software, it was made a web search of the GFP referred by the participant, and after, all nutritional profile of the products were added on the software, wherefore, it was followed the ingredient and the nutrition information provided by the manufacturer. For processed GFP reported, it was used the same brand for all those who reported have used the same type of product. For example, same type of gluten free white bread was used for all patients who reported intake of gluten free white bread. For fresh prepared meals or food, the nutritional profile was obtained based on the information of the ingredients given by the participants (Shepherd and Gibson, 2013). It was also defined which GFPs were most indicated by the non-compliant participants from the obtained result of analysis done.

Nutrients

To verify the adequate intake of macronutrients (carbohydrate, protein, fat), micronutrients (calcium, vitamins B6 and B12, total folate and iron) and fiber were used the dietary reference intakes (DRIs), such as, estimated average requirement (EAR) and adequate intake (AI). Total energy intake was determined according to estimated energy requirement (EER). Fiber energy density was evaluated according to recommended daily intake (RDI), and was classified as very low when energy density results were less than 0.6 Kcal/g; as Low when were between 0.6 to 1.5 Kcal/g; as medium when were between 1.5 to 4 Kcal/g; and as High when the outcomes were more than 4 Kcal/g (Stookey, 2001; Department of health Report and Social Subjects, 1991).

Anthropometry

Recent Weight and height were obtained through the hospital database.

Body Mass Index (BMI)

BMI was calculated using the following formula: weight (Kg) / height (m2) (Bardella et al., 2000). Next the BMI data were classified using the World Health Organization Criteria: BMI <18.5 kg / m2 (Underweight); BMI> 18.5 and to 24.9kg / m2 (Eutrophic); BMI> 25 and up to 29.9kg / m2 (overweight) and BMI> 30,0 kg / m2 (Obese) (Flegal *et al.,* 2010; Kabbani *et al.,* 2012).

3.4. **Procedure**

The ethical approval of this study was given both by University of Roehampton and Leicester General Hospital NHS Trust and was obtained through my supervisor. After that, this search started by analysing the database of the patients with CD in order to identify patients who are according to criteria for inclusion and exclusion pre-established. Then it was printed out the consent form, the questionnaire and the 3-day food diaries. After being read and explained about the aim and any doubts related to this study all participants gave their consent.

The PhD student has stamped the questionnaires and the 3-day food diaries with a reference number of identification to preserve the anonymity of the patients, and then has sent them by post with a return envelope. The participants also received with the questionnaire a message written in seven different languages informing that in case of they do not understand English, the researcher are available to clarify any doubts in their native language. The 3-day food diaries were sent with the use instruction and a guideline about how to measuring portion sizes. Demographic information and anthropometric measures were obtained by database of the hospital, and height and weight data were used to calculate the BMI. All data were collected between 2014 and 2015. All diaries data were analysed using diet plan software 6.0 and then reduced in nutrients. It was also identified the GFPs most mentioned by

non-compliant patients from the analysis of food diaries (Shepherd and Gibson, 2013). Lastly, all data collected were transferred to an excel template and then analysed using a Computer Package for Social Sciences (SPSS) version 21 available in the Roehampton University IT helpdesk.

3.5. **Ethics**

University of Roehampton and the authority of NHS Health Research gave the ethical approval, and the reference and protocol number are 14/LO/2128 and CD/RU/01, respectively (Appendix 03). Participants gave their consent and were informed that they were free to withdraw from this study at any stage. To maintain their anonymity, each of them was identified with a reference number.

3.6. **Statistical Analysis**

SPSS version 21 was used for statistical analysis, and statistical significance was considered at p value 0.05. Populations of the study were determined using descriptive statistics of which includes means, standard deviations (SD), median, range, correlation coefficient, frequencies and percentages. For describing the population, data were divided in two groups of variables: categorical that included gender, ethnicity, GFD on prescription, length of symptoms before GFD, frequency of gluten containing food inclusion in patients′ diet, meeting RNI-intake of nutrients, symptoms after GFD and type of symptoms after GFD (nausea, vomiting, mouth ulcers, stomach pain, fatigue, others); and continuous variables that involved age, weight, height, BMI, level of compliance and nutrients intake (carbohydrate, protein, fat, fibre, vitamin B6 and B12, calcium, total folate, iron).

Variables that were considered as independent were age, gender, ethnicity, weight, height, energy intake, nutrients intake (carbohydrate, protein, fat, fibre, vitamin B6 and B12, calcium, total folate, iron), GFD on prescription and source of gluten containing food, length of symptoms before GFD. As dependent were: BMI, meeting RNI-intake of nutrients, symptoms after GFD, type of symptoms after GFD (nausea, vomiting, mouth ulcers, stomach pain,

fatigue, others), level of compliance and frequency of gluten containing food inclusion in patients′ diet. Normality of the distribution was defined using Kolmogorov-Smirnov statistic.

For all differences analysis between compliant and non-compliant patients were used Mann-Whitney test and/or Chi-square test. The differences verified between these two groups were related to age, gender, ethnicity, weight, GFD on prescription and frequency of gluten containing food inclusion in patients′ diet. It was also identified differences in BMI, energy intake, type of symptoms after GFD (nausea, vomiting, mouth ulcers, stomach pain, fatigue, others), nutrients intake (carbohydrate, protein, fat, fibre, vitamin B6 and B12, calcium, total folate, iron) and meeting RNI-intake of nutrients. Correlation between BMI and energy intake, fat and fibre was done using Spearman′ and Pearson′ correlation tests. All tests were used in order to test and responding the hypotheses of this study: whether there are differences between compliant and non-compliant patients in nutritional intake, anthropometry and clinical presentation of the CD after following a strict GFD

4. RESULTS

4.1. Descriptive

By the time of data collection only 100 patients had sent the questionnaires and the food diaries but only 86 patients met all of both criteria for inclusion and exclusion. Thus, the participants constituted by 63 (73.3%) female and 23 (26.7%) male, aged between 19 to 64 years old (mean 46 / SD 14.5), and 95.3% were European, 1.2% were Muslim, 1.2% Sikh, 1.2% Hindu and 1.2% did not answer. The mean results of Weight and height were 74kg (SD 4) and 1.65 m2 (SD 6), respectively. Overall, the mean BMI results were 27.5 kg/m2 (SD 1.8). Table 01 shows a brief overview of results of age, gender, ethnicity, energy intake and BMI divided in two groups, compliant and non-compliant patients (Appendix 04).

Table 01. Mean and (SD) of demographic information, energy intake and BMI of compliant and non-compliant patients (Appendix 05).

COMPLIANCE GROUPS			
Compliant N= 71		**Non-compliant** N=15	
Age (years)	47.2 (14.3)*	**Age (years)**	42.9 (15.7)*
Gender (n)		**Gender (n)**	
Female	54	**Female**	9
Male	17	**Male**	6
Ethnicity % (European)	97.2	**Ethnicity % (European)**	86.7
Weight	74.6 (4.3)*	**Weight**	73.9 (4.9)*
Energy intake (Kcal/day)	1400 (364.5)	**Energy intake (Kcal/day)**	1342 (422.6)*

4.2. **Compliance with a gluten free diet**

Regarding to compliance with a GFD, according Leffler score, analyses demonstrated that the proportion of compliant patients (82.6%, 71 patients) was higher than non-compliant (17.4%, 15 patients). The mean Leffler score for compliance was 13.5 (SD 4) (Appendix 07). By analysing how often the patients include food-containing gluten on their diet, the results showed that most of reported answers were “never” by 69.8% and “once a month” by 15.1% (Figure 01). Findings related to GFD on prescription showed that 34.9% of patients answered did not receive, 62.8% that received and 2.3% answered the question as not applicable to them (Figure 02).

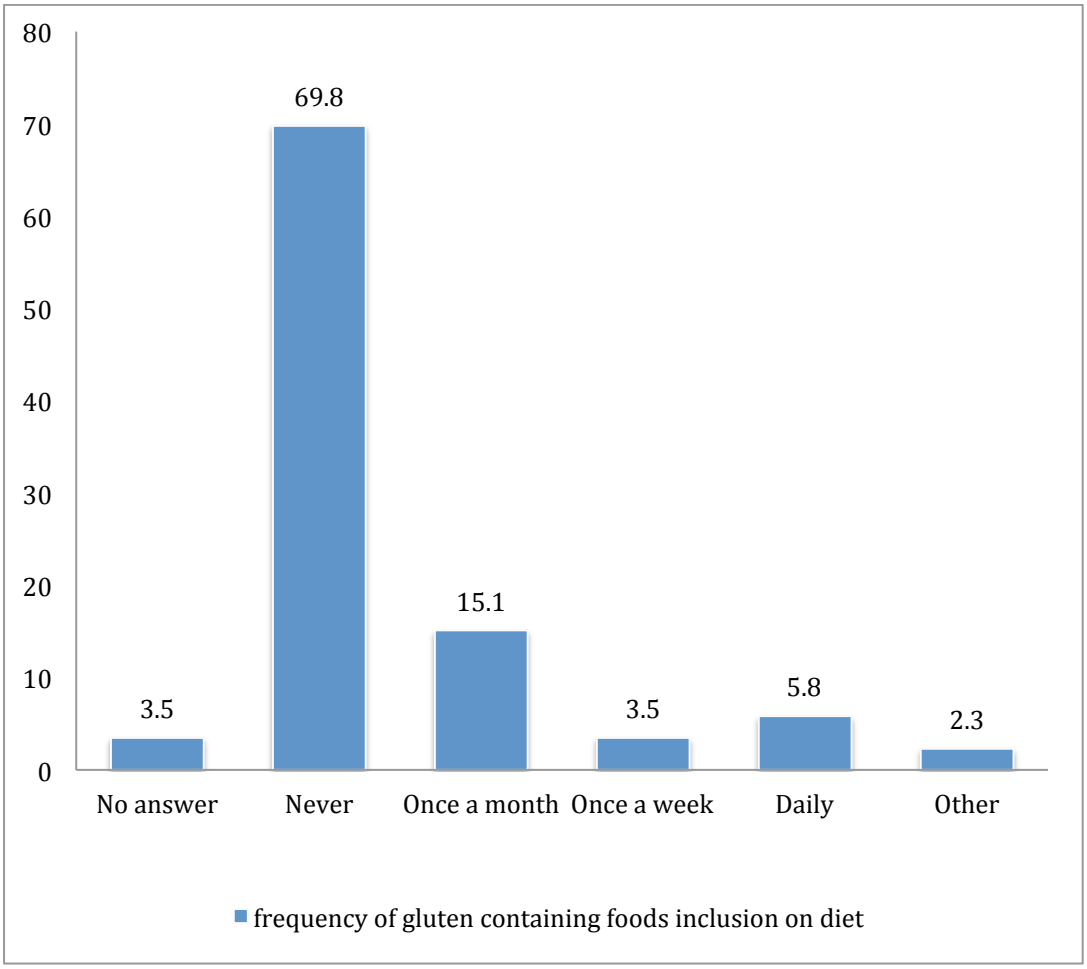

Figure 01. Frequency of consumption of products containing gluten in the diets of the patients (Appendix 06)

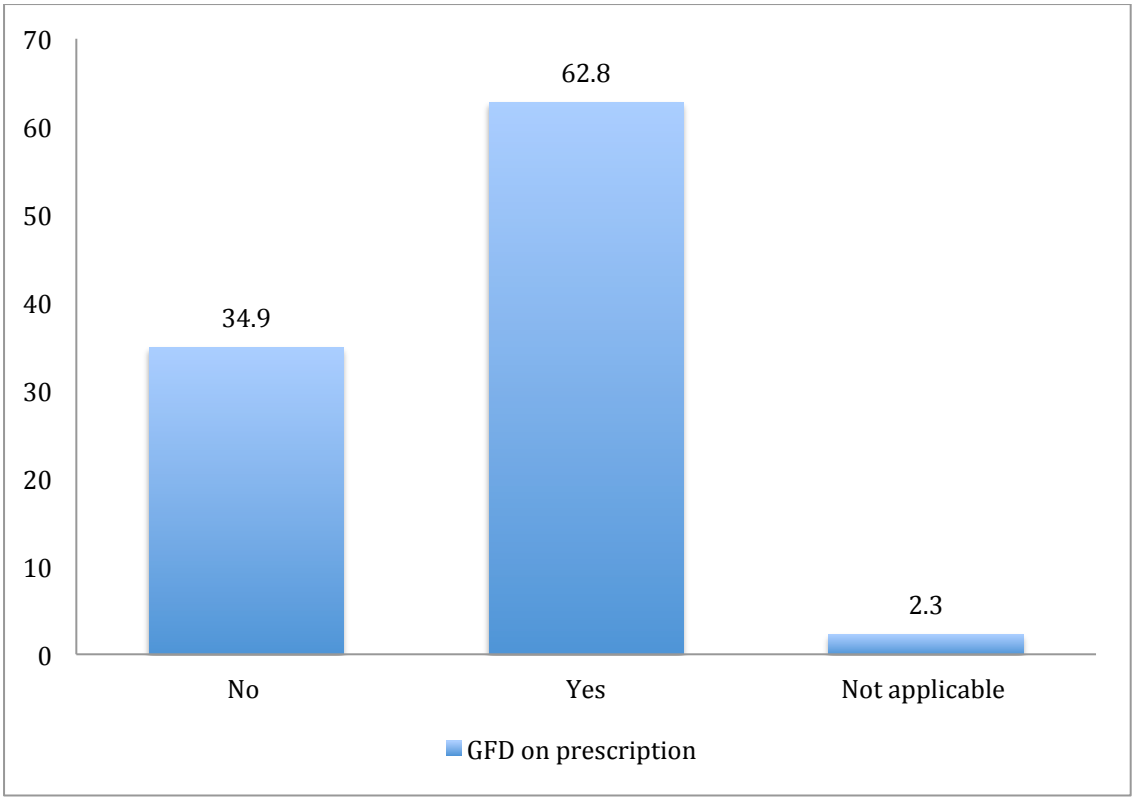

Figure 02. Distribution percentage of GFD on prescription (Appendix 06)

Table 02 shows the comparison between compliant and non-compliant in terms of age, gender, ethnicity, weight, GFD on prescription and frequency of consumption of products containing gluten in the diets. No significantly difference was found when was compared the two groups related to age (p=0.44) and weight (p=0.60). In both group the majority of the patients were female and European (compliant 76.1% female and 97.2% European; non-compliant 60.0% female and 86.7% European). There was a high difference related to percentage of students who reported have received GFD on prescription between compliant (33.8%) and non-compliant (40.0%). Regarding to frequency of consumption of products containing gluten on diet, 73.2 of compliant answered never included compared to 53.3% of non-compliant. The group of food that contain gluten in their composition eaten in transgression were bread, cereal, cake, pizza, biscuits, porridges, pasta, fish fingers, sausages and gravy.

Table 02. Values of difference in age, gender, ethnicity, weight, GFD on prescription and frequency of consumption of products containing gluten on diet between compliance groups (Appendix 07)

	Compliance groups		
Variables	**Compliant N=71**	**Non-compliant N=15**	*P*
Age (years)*	51 (45)**	42 (43)**	0.44
Gender (%) ***			
Female	76.1	60.0	
Male	23.9	40.0	
Ethnicity (%) ***			
European	97.2	86.7	
Muslin	---	6.7	
Sikh	---	6.7	
Hindu	---	---	
No answer	1.4	---	
Weight (Kg)*	73.7 (16.7)**	72.7 (17)**	0.60
GFD on prescription (%)***			
Yes	63.4	60.0	
No	33.8	40.0	
Not applicable	2.8	---	
Frequency of consumption of products containing gluten on diet (%)***			
No answer	4.2	---	
Never	73.2	53.3	
Once a moth	12.7	26.7	
Once a week	2.8	6.7	
Daily (%)	4.2	13.3	
Other (%)	2.8	---	

*Man Whitney statistic test; ** Median and (range); *** Chi-square test

4.3. **Dietary intake**

On the Table 03 is represented the results of the dietary intake of the patients. Energy intake mean was of 1390 Kcal/day (SD 373.2), which is not according to EER. The mean of carbohydrate intake (168.8 g/day, SD 55.8) was above of EAR and mean fat intake (54.1 g/day, SD 18.1) was normal compared to AI recommendation. Protein mean intake was 51.3 g/day (SD 13.4), which is under of EAR daily recommendation. The fibre intake and fibre energy density results are lower than recommended by AI and DRIs, 14.5 g/day and 1.06 g/day, respectively. Amongst the micronutrients, the mean value of vitamin B6 (1.2 mg/day) calcium (492.2 mg/day), total Folate (157.8 mg/day) and iron (6.0 mg/day) are below the recommended level by EAR and AI, unlike the mean value of the vitamin B12 is above (2.96 mg/day) (Appendix 08).

Table 03. Results of macronutrients, fibre and micronutrients intake, and fibre of CD patients: Mean and recommendation of nutrients intake (RNI).

Nutrients intake	**Mean (RNI, Department of health Report and Social Subjects, 1991)**	**Std. Deviation**
Energy intake (Kcal/day)	1390.3 (1600-2000 Kcal/day)	373.3
Protein (g/day)	51.3 (64 g/day or 0.8g/Kg)	13.3
Fat (g/day)	54.1 (53 g to 65 g/d)	18.1
Carbohydrate (g/day)	168.8 (130 g/day)	55.8
Fibre (g/day)	14.5 (25 g to 30 g/day)	5.3
Vitamin B6 mg/day)	1.2 (1.3 mg/day)	0.4
Vitamin B12 mg/day)	2.96 (2 mg/day)	3
Calcium mg/day)	492.2 (1000 mg/day)	257.6
Iron mg/day)	6.0 (8 mg/day)	2.9
Total folate (mg/day)	157.8 (320 mg/day)	76.9
Fibre energy density (g/day)	1.06 (> 4 Kcal/g)	0.4

Figure 03 demonstrates a summary of the percentages of meeting RNI-intake of fibre, vitamin B6, Vitamin B12, calcium, Iron and total folate. The results show that 67.4% of the patients meet the recommendation intake of Vitamin B12 intake. However, the percentage of those that did not meet intakes is higher when it comes to other studied nutrients: fibre 95.3%, vitamin B6 65.1%, calcium 96.5%, iron 83.7% and total folate 98.8% of patients.

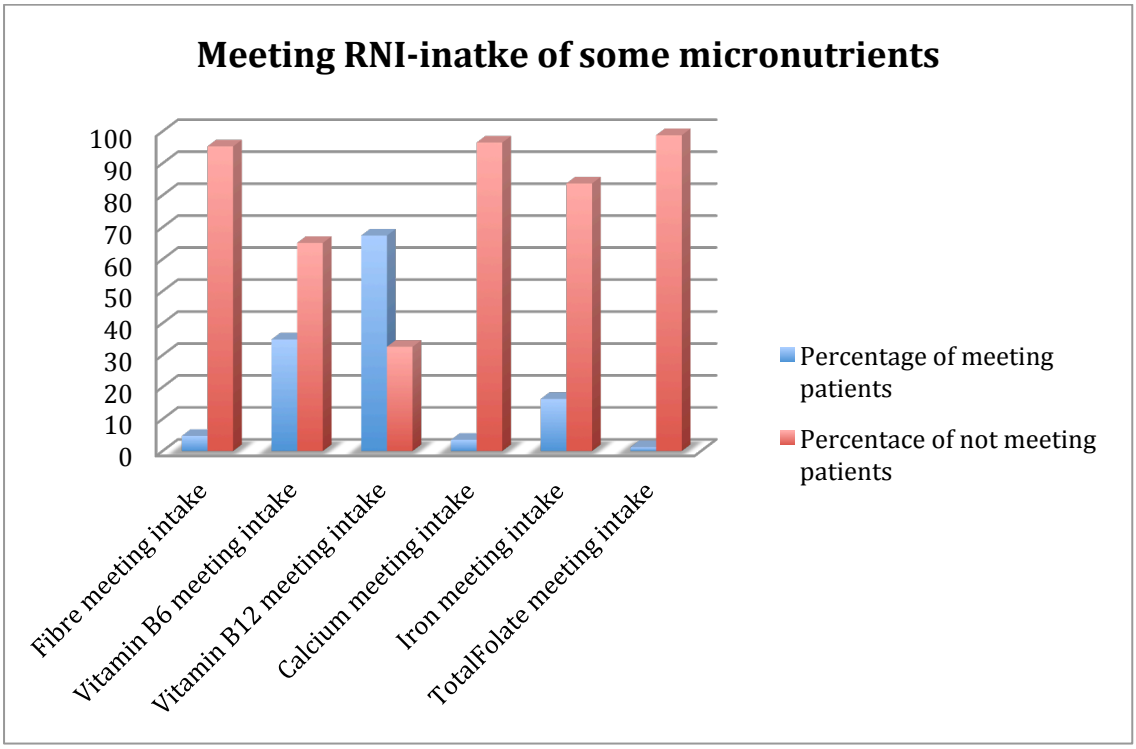

Figure 03. The percentages of meeting intake of fibre, vitamin B6 and B12, calcium, iron and total folate of the CD patients (Appendix 08)

There was no significant difference in consumption of energy intake, macronutrients (energy intake p=0.470, carbohydrate p=0.785, protein p=0.163, fat p= 0.406) and fibre (fibre p=0.076) between compliant and non-compliant patients. As well as, no significant difference was found amongst micronutrients between the two groups (vitamin B16 p=0.746, vitamin B12 p=0.470, iron p=0.342, folate p= 0.524 and calcium p=0.082) (Table 04). Nevertheless, it was found a high difference between compliance groups related to energy density of the fibre (p=0.029). Table 05 shows the meeting RNI-intake of nutrients of compliant and non-compliant patients, as it is possible to see, 94.4% of compliant and 100% of non-compliant did not meet

the RNI-intake of fibre. Meeting RNI-intake of vitamin B6 was seen in 35.2% of compliant and 33.3% of non-compliant; meeting RNI-intake of vitamin B12 in 66.2% of compliant and 73.3% of non-compliant, and meeting RNI-intake of iron in 14.1% of compliant and 26.7% of non-compliant. Comparing meeting RNI-intake of calcium and folate between groups, 100% of non-compliant patients did not meet the RNI-intake for both micronutrients; and 95.9% of the compliant patients meet RNI-intake for calcium and 98.6% for folate.

Table 04. Difference between compliance groups related to macronutrients, micronutrients, fibre and energy density of fibre: median, range and p value (Appendix 09).

Nutrients	**Compliance groups**		Difference between compliant and non-compliant
	Compliant	**Non-compliant**	
	Median (range)		*P**
Energy intake (Kcal/day)	1329 (1822)	1279 (1719)	0.470
Carbohydrate (g/day)	159.3 (313)	159.7 (163.3)	0.785
Protein (g/day)	50.4 (80.4)	43.2 (41.0)	0.163
Fat (g/day)	51.2 (92.9)	58.8 (60.8)	0.406
Fibre (g/day)	14 (26.4)	12.5 (15.7)	0.076
Vitamin B6 (mg/day)	1.1 (2.1)	1.1 (1.3)	0.746
Vitamin B12 (mg/day)	2.5 (26.1)	3.3 (5.2)	0.470
Calcium (mg/day)	467 (1900)	378 (553)	0.086
Iron (mg/day)	5.5 (14.0)	6.0 (8.4)	0.342
Total folate mg/day)	155 (442)	142 (196)	0.524
Fibre Energy density (g)	1.0 (1.86)	0.86 (0.87)	0.029

* Man Whitney statistic test

Table 05. Difference between compliant and non-compliant patients related to meeting RNI-intake of fibre and micronutrients (Appendix 10).

	Compliance groups	
Meeting RNI-intake of nutrients	**Compliant**	**Non-compliant**
	N (%)	
Fibre (g/day)*		
Yes	4 (5.6)	---
No	67 (94.4)	15 (100)
Vitamin B6 (mg/day)**		
Yes	25 (35.2)	5 (33.3)
No	46 (64.8)	10 (66.7)
Vitamin B12 (mg/day)**		
Yes	47 (66.2)	11 (73.3)
No	24 (33.8)	4 (26.7)
Calcium (mg/day)**		
Yes	3 (4.2)	---
No	68 (95.8)	15 (100)
Iron (mg/day)**		
Yes	10 (14.1)	4 (26.7)
No	61 (85.9)	11 (73.3)
Total folate mg/day)**		
Yes	1 (1.4)	---
No	70 (98.6)	100

* Chi-square test

4.4. **Nutrition status of the patients**

Correlation between BMI and energy intake of patients revealed that although the correlation coefficient (0.304) indicates that the relationship between these two variables is weak, the values of P says that correlation is significant

(p=0.004). A weak but significant correlation between BMI and fat and fibre were also found, p= 0.026 and p=0.041, respectively (Table 06). Figure 04 shows that the BMI increase relatively with the increase of energy intake. The BMI mean of compliant patients were 27.7 (SD 1.8) and non-compliant patients was 26.6 (SD 1.7). The BMI between the groups was highly different (p=0.048) (Table 07).

Table 06. Correlation between BMI and fat, fibre and energy intake (Appendix 11)

	Correlation
	P (r)
BMI and energy intake	0.004 (0.304)**
BMI and fat	0.026 (0.241)*
BMI and fibre	0.041 (0.220)*

*Spearman's′ correlation test

*Pearsons′ correlation test

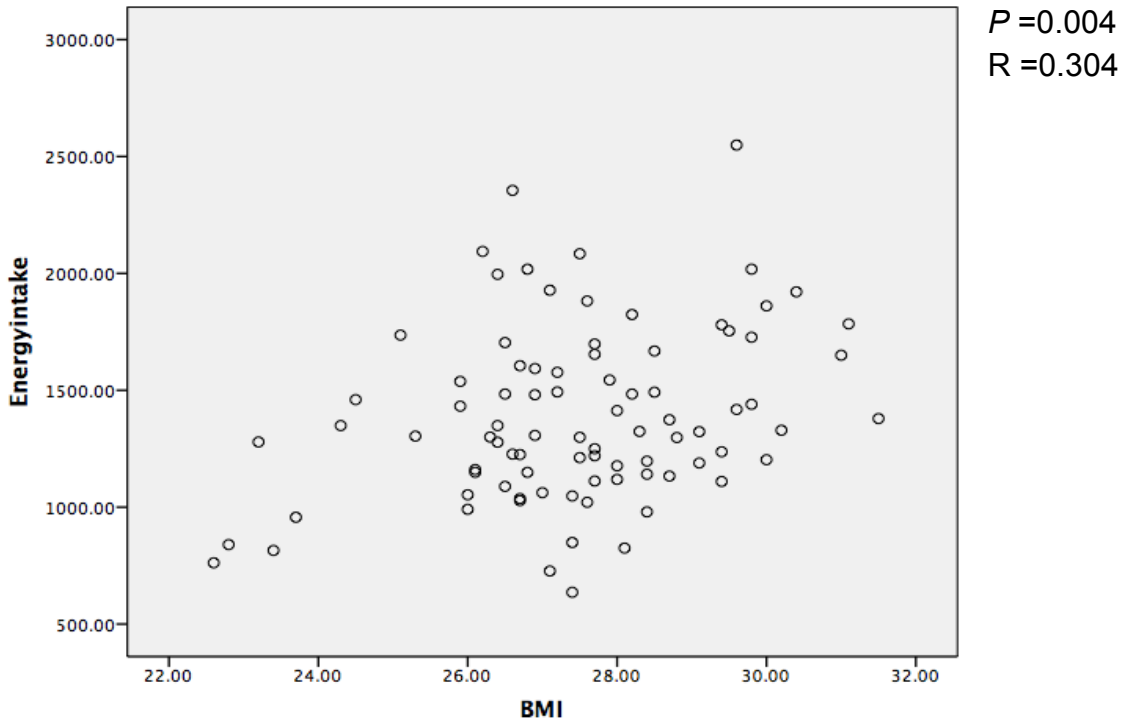

Figure 04. Result of correlations between BMI and energy intake (Appendix 11)

Table 07. BMI mean and SD of compliant and non-compliant patients, and the difference in BMI between the two groups (Appendix 11)

Nutritional parameter	Compliance group		Difference between the groups
	Compliant	Non-compliant	
	Mean (SD)		*P**
BMI (Kg/m^2)	27.7 (1.8)	26.6 (1.7)	0.048

* Man Whitney statistic test

4.5. Symptoms before and after GFD adherence

Regarding to length of symptoms before adherence to GFD, 36% of the patients reported symptoms for “more than 3 years “, 29.1% for “1 year to 3 years”, 18.6% for "6 months to 1 year", 12.8% for “less than 6 months", 2.3% answered "other" 1.2% did no answer (Figure 05). The percentage of patients with symptoms after GFD treatment was of 82.6%. Percentage of those that reported no symptoms after GFD was of 7%, and “not applicable” was stated by 10.5% (Figure 06).

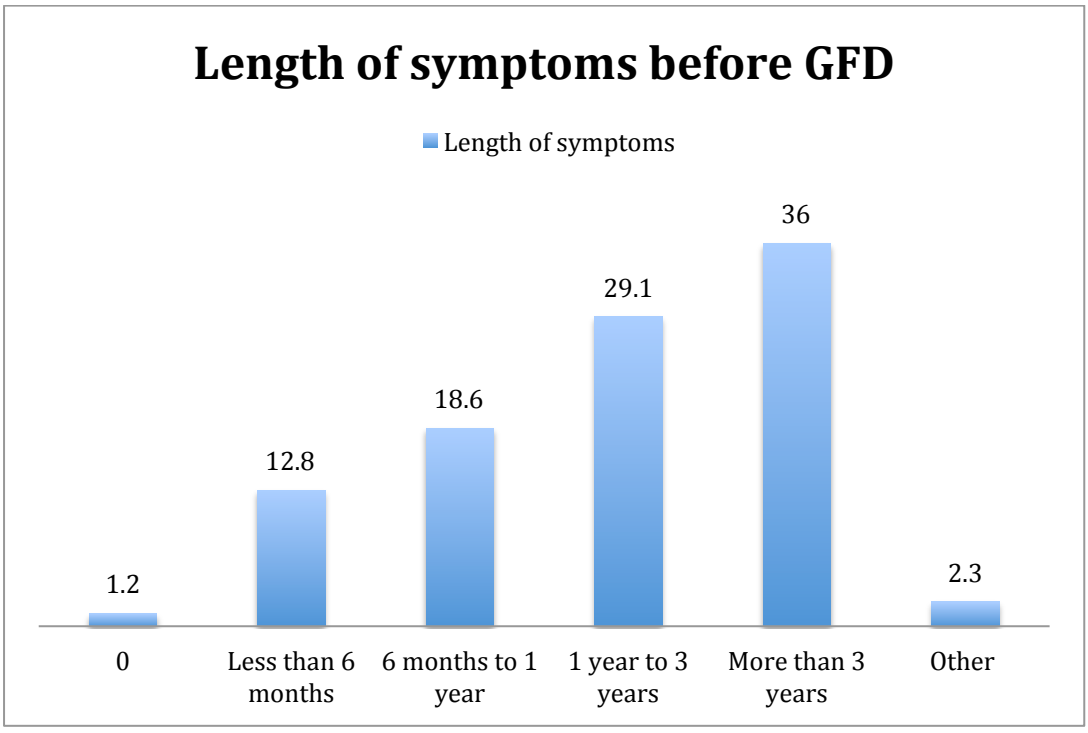

Figure 05. Length of symptoms before GFD (Appendix 12)

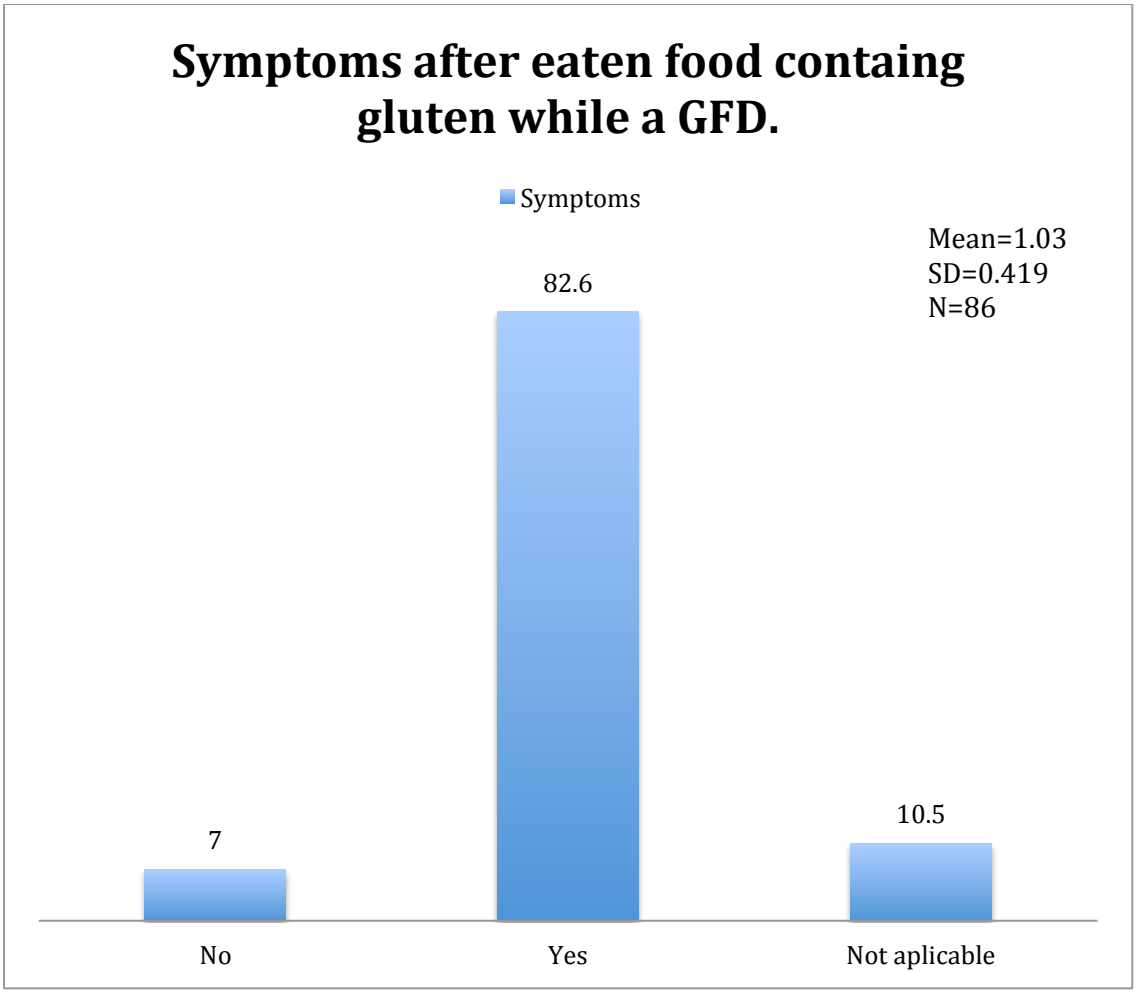

Figure 06. Symptoms after introduction of GFD (Appendix 13)

The types of symptoms reported by compliant and non-compliant patients are represented on Table 08. Fifty-two compliant patients reported nausea and Vomiting and mouth ulcers by 63 of them. High number of compliant (59 patients) reported do not have symptoms as they do not eat food-containing food. Regarding to non-compliant, 11 of them reported fatigue, 9 nausea and vomiting, and diarrhea, and 13 of them said do not have symptoms.

Table 08. Types of symptoms mentioned by compliant and non-compliant patients (Appendix 13).

		Compliance groups	
Symptoms *		**Compliant** **N=71**	**Non-compliant** **N=15**
Nausea and vomiting	No	52	09
	Yes	19	06
Diarrhea	No	36	09
	Yes	35	06
Fatigue	No	39	11
	Yes	32	04
Mouth ulcers	No	63	13
	Yes	08	02
Stomach pain	No	36	06
	Yes	35	09
Not applicable: do not eat gluten containing food and hence do not know	No	59	13
	Yes	12	02
Others	No	50	11
	Yes	21	04

***** Chi-square test

5. DISCUSSION

5.1. Compliance with gluten free diet

It is highly recognized that treatment for celiac disease is based exclusively on GFD, which have to be strict and for a lifetime (Castillo *et al.,* 2014). Individuals with CD may find that GFD is an overwhelming responsibility and extremely burdensome for them (Hopper *et al.,* 2007). Therefore, compliance with a GDF has been considered a major challenge, even more recently due to increasing growth of diagnosis (Errichiello *et al.,* 2010). Monitoring whether the CD patients are complying with GFD is certainly an important aspect of long-term CD management (Green *et al.,* 2015; Biagi *et al.,* 2009).

In this research, compliance with a GFD was extremely higher (82.6%), as well as, non-compliant group (17%) was much high compared to others published studies. Sainsbury *et al.,* (2013) in a recent study using the same Leffler's questionnaire to assess adherence to GFD with 390 CD adults' participants found that 52.7% of them reported excellent adherence to GFD, 37.2% moderate adherence and 6.2% fair to poor adherence. Similarly, Rubio-Tapia *et al.,* (2010) assessed compliance to GFD, using dietician interview with 241 patients and showed that 66% of those assessed had good compliance, 21% moderate and a poor compliance was found in only 13% of them. Leffler *et al.,* (2007) demonstrated in their study with adults CD only the rates of excellent and good adherence to the GFD, which were 44.2% and 34.4%, respectively. A high adherence rate to GFD was also shown in other prospective studies. For example, a prospective study with 490 participants compared three study groups in terms of self-rated adherence to GFD. The rates of adherence were elevated in the three groups: patients with classic symptoms had 85% of adherence, those with extra-intestinal symptoms 78% and the screen-detected group had 91% of adherence (Ukkola *et al.,* 2011). Viljamaa *et al.,* (2005) verified dietary compliance in 53 screen-detected patients with 14 years of followed-up and in 44 symptom-detected patients with 10 years of followed-up, through an interview made by an experienced dietician. The study found that 83% of screen-detected patients has followed a strict GFD and 14 % a fairly strict GFD, and in the same way, 77% of

symptom-detected participants kept a strict GFD and 16% a fairly strict adherence. Despite many studies has been shown good rate of compliance, it is noticeable that the choice of methods used to measure adherence to GFD may influence negatively the results by overestimating their adherence, for example, self-reported method, which may not be completely reliable, since the patients may report an inaccurate self-assessment (Biagi *et al.,* 2009). On the other hand, Sainsbury and Mullan (2011), who measured behavioural beliefs related to GFD adherence in CD individuals demonstrated that there is a significant relationship between intention to maintain a strict GFD and adherence to GFD. They suggested that many patients believe that the advantages of a strict gluten-free diet are the main reasons that lead them to maintain the diet compared to the disadvantages. Furthermore, they showed that poor GFD adherence is related to increased concern of the patients in avoiding any inconvenience or offences that they might cause to others. Poorer adherences, as well as, lower intention were associated with belief that it is easy to have a balanced gluten free diet. Due to these findings the authors reported that is necessary to monitoring the diet of the patients to prevent possible exposure to gluten.

Factors related to compliance with a GFD were not methodically analyzed in this study. However, voluntary dietary transgression was identified in a representative number of patients who reported to include food-containing gluten on their diet, and this occurred more among non-compliant patients (22.5% of compliant, 46.7 of non-compliant). Our findings are consistent with Shepherd and Gibson, 2013. In their study were compared 55 patients who were on a GFD over than 2 years to 50 newly diagnosed. Overall, was found that 75% of patients were following strictly a GFD, in which 10% of those patients reported inclusion of gluten containing food unconsciously and 23% reported to consume gluten occasionally. In a 5 years-study was determined adherence to GFD and was evaluated its strictness. Food frequency questionnaire was used as method interview in 95 adults with CD, and patients were divided in 3 groups: group A no detected transgression, group B moderate transgression and group C large transgression. This research found no transgression in 40 compliant patients (group A) and transgressions in 55

non-compliant patients (group B and C). Among non-compliant, 38 patients identified the transgression as intended and 17 as unintentional. Patients reported some reasons for voluntary transgression, such as, absent of symptoms after ingestion of GFPs, GFPS are less tastiness than habitual food, GFPs are more expensive, cultural reasons, and GFD brings more restrictions than benefits. Unintentional transgression were justified by pharmaceuticals that (Vahedi *et al.,* 2003). Errichiello *et al.,* (2010) found dietary lapses among CD patients in a study with adolescent and young adults patients. Among 204 patients, 73.5% of them did not committed dietary transgression but 26.5%, which is similar to our study, admitted frequent or occasional dietary transgression. A Brazilian study with 105 CD patients, in which 90.4% were on GFD also found that significant percentage of their participants (67.1%) consumed gluten containing food involuntarily or due to lack of food options/ or food information available in public space (Araujo and Araujo, 2011). Types of food containing gluten consumed in transgression were mostly processed food, and this was also mentioned in a prospective study of Errichiello *et al.* (2010). Their outcomes shown that snack, including sweets, and bread were the sources of food containing gluten most reported in transgression by 38.9% of 54 patients. These findings are consistent with Araujo and Araujo, (2011) and Leffler *et al.* (2008), who mentioned a number of factors that were related to consumption of these food containing gluten, such as, limited alternatives at food shops, alternatives foods require extra spare time and energy to be prepared, lack of food manipulation and culinary skills, limited financial resource and difficulty of finding adequate menu for the family, and difficulty to vary the diet.

There are few consistent studies that examined difference related to demographic information between compliant and non-compliant participants (Errichiello et al., 2010; Hall et al., 2009). In this present study, higher number of patients were female in both groups but percentage of compliant female patients (76.1%) were bigger than non-compliant (60%), and non-compliant male patients (40%) were higher than male compliant (33.8%). Regarding to ethnicity, 97.2% of compliant were European compared to 86.7 of non-compliant (p=0.031). Errichiello et al., (2010), for example, did not find any

difference between genders or among age groups related to compliance with GFD. Kratzer et al., (2013) verified CD prevalence in 2157 German participants. This prospective study revealed 52% of them were women and 48% men. High prevalence of white and female (76.6%) patients with CD were reported in other prospective study, where was compared five methods of measuring adherence to GFD in adults patients aged over 18 years old. This study also showed that all patients treated at the Medical centre selected for that study were female and white (71.7%). Additionally, an expert nutritionist reported that female demonstrated lightly better GFD adherence (Leffler *et al.,* 2007). Butterworth *et al.* (2005), compared factors that are related to compliance with a GFD between white Caucasian (n=66) and South Asian (n=21) CD patients. They found that large percentage of white Caucasian (74%) was on a strict or moderately strict GFD compared to South Asian (66.6%). Results of another study carried out by Kabbani et al., (2012) demonstrated that good and poor adherence was mostly amongst white populations and females. Good adherence was described in 77% of female participants and in 94% of white populations, and the mean age was 52.2 years old. Poor compliance was reported in 72% of female and in 97% of white populations and the mean age was 53 years old. Therefore, as various studies with CD patients have demonstrated majority of CD patients are white, female and with European ancestry (Casellas et al., 2006; Ludvigsson et al., 2014; Perreira *et al.,* 2006).

Despite this study did not find difference in the answers related to GFD on prescription between groups, this study verified that the percentage of non-compliant patients (40.0%) who reported not be given GFD on prescription was higher than the compliant patients (33.8%). In a recent study Tennyson et al. (2013) measured the interest level of 465 patients related to the use of medication in the treatment of CD using a Coeliac Dietary Adherence test. When patients were asked how often a dietician saw them, only 5% answered regularly compared to 20% of those who answered have never been seen by a dietician. Moreover, in another recent study, 7% of 113 patients reported did not receive any follow-up for CD. Authors also found that 35% of them were considered to have a consistent follow-up, which was according to American

Gastroenterology Association, and 58% had an inadequate follow-up for CD. Furthermore, they suggested that a practise of inadequate monitoring tends to affect negatively the long-term positive effects of GFD compliance (Herman *et al.,* 2012). Nevertheless, Some doctors do not understand the importance of a strict and lifelong GFD, and consequently they might not prescribe GFP to their patients. All patients should be advised regularly, from the first consultation on the importance of adhering and maintaining a GFD for lifetime. Since, it is suggested that compliance with GFD can be improved through an adequate follow-up (Butterworth *et al.,* 2004).

5.2. **Dietary intake**

A few studies have investigated the nutritional status of CD patients, the GFD nutritional quality and the influence of non-compliance, mainly, using dietary questionnaire (Kinsey *et al.,* 2008). Dietary inadequacies is a common condition in CD and the nutrients most mentioned by many studies are iron, vitamin B12, calcium, folate, fibre, energy intake and macronutrients (Moreno *et al.,* 2014; García-Manzanares and Lucendo, 2011). Therefore, It has demonstrated that it is extremely important for the health professionals, which work with nutrition education of patients with CD, to know whether gluten free diet is sufficient for CD individuals in order to meet its dietary or nutritional recommendations, as well as, to know the impacts of nutritional inadequacies on CD individuals health (Shepherd and Gibson, 2013). Findings of this study demonstrated that patients had low intake of protein, fibre, energy density of fibre, and todal energy intake, compared with the DIRs. However, it was found a higher intake of energy as carbohydrate, and the mean fat intake was according to the recommendation. Concerning to studied micronutrients, Vitamin B12 was the only above the nutritional recommendation. No significant difference was found in all macronutrients, micronutrients, and fibre intake between compliant and compliant, except fibre energy density. Meeting intake of nutrients were also analysed in our study. The percentage of patients who failed to meet RNI-intake of fibre, vitamin B6, calcium, iron and total folate were significantly above of those that meet the recommendation intake. Regarding to vitamin B12 the percentage of patients who meet the

RNI-intake was higher. All non-compliant patients did not meet RN-intake of calcium, folate and fibre. Additionally, percentage of non-compliant patients who did not meet RNI-intake of all micronutrient studied were higher then compliant patients, except for vitamin B12 that was higher amongst non-compliant.

Comparably, Ghen *et al*. (2001) showed the overall nutrient intake of 49 patients aged between 45 to 64 years, on a GFD for 10 years. The mean daily intake of vitamin B6 (female 1.7 g/d, male 1.9 g/d), vitamin B12 (female 4.3 g/d, male 5.3 g/d), Calcium (female 837 g/d, male 999 g/d) and carbohydrates (female 220 g/d, male 254 g/d) were considered high in both gender. Total Energy intake (female 220 g/d, 254 g/d) was according to Nordic Nutrition Recommendations (NNR). Folate (female 186 g/d, 172 g/d) and fibre (11.5 g/d, 10 g/d) were lower than the recommendation. Hallert *et al.* (2002) carried out a study with 30 adults with CD, on a GFD for 10 years. They aimed to verify the prevalence of vitamins and mineral deficiency amongst those patients. Patients had a low mean daily folate intake (184 mg/d) and higher intake of vitamin B6 (1.8 mg/d) and vitamin B12 (5.1 mg/d). All values were compared to NNR. Moreover, they also correlated vitamin intakes with plasma levels but the correlations were weak ($r < 0.18$). Bardella et al. (2000) found high total energy intake amongst male (2314 Kcal/d) and normal amongst female (1609 Kcal/d). This study also indicated high consumption of fat and low of carbohydrates. Most recent study related to nutritional inadequacies in CD patients found that patients who were on GFD for 2 years had elevated intake of iron (male 15.8 mg/d, female 11.9 mg/d), calcium (male 909 mg/d, female 987) and total fat (67.9 g/d, 72.7 g/d), compared to AI and EAR. Energy intake (male female 2697 Kcal/d, 2040 Kcal/d), Carbohydrate (male 294 g/d, female 236 g/d) and protein (male 98.8 g/d, female 89.2 g/d) also exceeded the recommendation. Total folate (male 403 mg/d, female 316 mg/d) and fibre (male 30 g/d, female 22 g/d) were high only amongst male. Furthermore, fat and protein reached the recommendation for female (68.3 g/d and 62.5 g/d) but were exceeded for male (92.1 g/d and 81.4 g/d). It were also demonstrated the number of patients with CD who did not reach levels of recommendations of some nutrients. Forty-nine patients failed to meet the

recommendations of fibre, 16 of vitamin B6, 48 of folate and 19 of calcium. Similarly another prospective study analysed the nutritional state as well as the nutritional management of GFD in CD patients aged 12-25 years old. All patients were found to have significantly lower intake of iron and fibre compared to Dutch and American recommendations. Patients older than 19 years reached the American recommendation for calcium. Vitamin B6 values were above the Dutch recommendation. Additionally, 64% of them reported make use of GFPs fortified with vitamins and minerals and 47% stated using supplementation of those nutrients (Hopman *et al.,* 2006). Despite studies have shown continues malnutrition amongst patients with CD even after using fortified GFPs and supplementation, it has been proposed that supplementation can be used for purposes of increasing the nutritional content in many gluten free products (GFPs) and as well as to increase nutritional intake in patients with the coeliac disease (Korus et al., 2009; Hallert *et al.,* 2009; Penagini *et al.,* 2013; Reilly *et al.,* 2012). Another suggestion would be a new dietary approach as dietary modification, which includes new variants of wheat and detoxification of gluten (Rashtak and Murray, 2012).

Although there is no published research addressing in detail about factors associated to nutrients inadequacy in individuals with CD even after GFD, few studies suggested some causes (Bardella *et al.,* 2000; Moreno *et al.,* 2014; Comino *et al.,* 2012; Rubio-Tapia *et al.,* 2010). It has been suggested that most of CD patients do not react positively to a GFD and possibly continues to have villous atrophy and then persistent malabsorption (Comino *et al.,* 2012; Rubio-Tapia *et al.,* 2010). Lanzini *et al.* (2009) found that despite adherence to GFD, it is extremely rare to find complete recovery of the duodenal impairment in adults with CD. Once the authors reported that after approximately 1 year and 3 months, only 8% of 465 patients had total histological duodenal recovery, 65% obtained remission and 26% remained the same. These findings discredit the possible benefits of GFD that have been highlighted by many studies for example, correction of nutritional loss or malnutrition (Haines *et al.,* 2008). However, it has been also shown that poor compliance or non-compliance to GFD may influence the dietary intake of CD

patients (Kinsey *et al.,* 2008). Voluntary consumption of foods containing gluten may be the reason for persistent injuries of the intestinal mucosa found in a perspective study with 236 participants with CD. This study showed that while 89 of them obtained recovery in the intestinal mucosa, 147 continued to have persistent injury, when was assessed the first follow-up biopsy. It was also demonstrated that amongst those patients with mucosal recovery, 75% was with good compliance, 20% was with moderate compliance and 4% with poor compliance to GFD. On the other hand, high level of non-compliance was found amongst those with persistent injuries of the intestinal mucosa. Good compliance was 61%, moderate 21% and poor compliance 18% (p=0.003) (Rubio-Tapia *et al.,* 2010). Araujo and Araujo (2011) also evaluated adequacy of nutrients intake after introduction of a strict GFD. Thus, It was correlated gluten-free dietary tracking with nutrients and energy recommended for a good health, and a significant association was found as p=0.0315. The study concluded that patients who tried to not consume gluten-containing food obtained a proper amount of nutrient and calories in their diet. Dietary inadequacy was also related to poor quality of GFD recommend currently, which do not provide adequate nutrients (Mearin *et al.,* 2005). Since, when it is introduced GFD in patients' lives occurs the elimination of some important foods that are rich in calcium, thiamine, niacin, protein, carbohydrates and energy, and it is also known that great part of processed foods have gluten and also need to be eliminated. All this can have a huge influence on nutritional contents of foods as was reported for many studies, and mainly, when there is no a good alternative for these products (Kinsey *et al.,* 2008; Moreno *et al.,* 2014). Thus, rigorous follow up and nutritional education, which includes food choice and composition, is important for prevention of malnutrition (Bardella *et al.,* 2000).

Although, various studies have shown persistent deficiency of nutrients after introduction of GFD (Grehn *et al.,* 2001; Hallert *et al.,* 2002), a prospective study has demonstrated a good clinical response to GFD in context of nutritional inadequacy (Caprisco *et al.* 2000). Interestedly, in a later study with 39 adults CD, Caprisco *et al.* (2000) compared macronutrient and micronutrients intake between treated and untreated CD patients. It was found

that energy intake and carbohydrate did not vary significantly between groups, as energy intake and carbohydrate of treated were 8400 kJ/d and 4500 kJ/d, and untreated were 8300 kJ/d and 4600 kJ/d. However, the results showed that treated patients had an elevated intake of fat (2300 kJ/d) than untreated (2150 kJ/d), and protein intake was equal (1500 kJ/d). Micronutrients amongst treated CD were also higher than untreated: iron 12.6 moll/L and 7.6 moll/L, vitamin B12 311 mmol/L and 294 mmol/L and folic acid 17 mmol/L and 11.8 mmol/L, respectively. It was also possible to verify that treaded patients had higher consumption of protein (89.5 g/d of protein) and carbohydrates (268.8 g/d of carbohydrates) and normal intake of fat (61g/d of fat) and total energy intake (2006 Kcal/d), when compared with the DRIs. Micronutrients were all according to the biochemical references values. However, it is important to emphasize that micronutrients were assessed using laboratory index, which comparing to dietary intake questionnaires, are more accurate regarding to the outcomes (Subar *et al.,* 2003). Even though it was used in this present research the same methodology (3-day food diary) as other studies, underreported were noticeable, may suggest that during this study occurred alterations in usual food patterns of the participants (Hallett *et al.,* 2002).

5.3. **Nutrition status of the patients**

Recently, alterations in the CD clinical presentation have been indicated by various studies, which is now characterised by increasing overweight or obese prevalence amongst individuals with CD (Rybak *et al.,* 2014). Likewise, this trend was observed in the present research, as both compliant and non-compliant CD patients were found overweight. In addition, BMI of compliant patients was significantly higher than non-compliant ($p=0.048$). As this study, many other are concerned about the nutritional status of patients with CD. Tucker *et al.* (2012) in a study analysed 240 CD adults who attended a Dietetics institution for 10 years (1999 to 2009). The study demonstrated normal BMI in 53% of them and underweight in 3% but there was a significant percentage of overweight (44%). The Increase in overweight or obese occurred along with the increase in the numbers of patients, as while in 2002

were only 4 patients (25% of obese), at the time of study (2009) the number has increased to 52 patients (73% of obese). Dickey and Kearney, 2006 verified BMI in 188 compliant CD patients who were on a GFD for 2 year. The BMI mean was 25.9, and with introduction of GFD 81% of those patients gained weight but 28% lost and 4% remained with same BMI. Gains of further weight were reported in patients who were initially overweight. Therefore, the number of overweight increased from 67 patients to 95, and also had an increase of obese patients, as 11 overweight patients and 2 who were in the normal BMI became obese. However, despite increasing overweight and obese, all studies that addressed the BMI of celiac patients have shown improvement in Body weight of these patients, while on GFD (Pulido *et al.,* 2013; Nachman *et al.,* 2010). Additionally, case of stable BMI in CD patients was also reported in celiac patients, after specialized follow-up or good management of GFD (Ukkola *et al.,* 2012; Bardella *et al.,* 2000; Reilly *et al.,* 2012; Kabbani *et al.,* 2012). Nachman *et al.* (2010), made a comparison between BMI of patients at 1 year of follow-up and 4 year of follow-up. Results showed a significant improvement in BMI of patients at 12 months of follow-up ($p<0.0002$), which maintained constant at 4 years of follow-up. A prospective cohort that was published in 2012 by Ukkola *et al.* assessed the influence of GFD on BMI, after 12 months of GFD introduction. Before GFD, 4% of 689 were classified as underweight, 57% of as normal, 28% as overweight and 11% as obese. After GFD, while underweight patients (69%) increased their body weight, those with overweight (18%) and obese (42%) had a decrease in weight. This positive effect of GFD on patients BMI was reported in both screen-detected and symptom-detected patients. However, despite it was seen positive changes in BMI, it seems that those changes were not related to dietary counselling given by heath professionals but with self-reported experiences on GFD and age at the diagnosis (young). Shepherd and Gibson, (2013) found an increase of mean BMI in newly diagnosed patients after 1 year on GFD. Female increased from 22.9 kg/m^2 to 24.4 kg/m^2 and male from 23.4 kg/m^2 to 25.5 22.9 kg/m^2, but male patients became slightly overweight. Experienced patients (2 years on GFD) were found with normal BMI. The mean BMI was of 24.2 kg/m2 and 25.0 kg/m2 for female and male, respectively. However, The two groups of patients did not differ significantly in

BMI. Similarly, this normal BMI were demonstrated in Bardella *et al.* (2000) study. They found only 7 patients with overweight, 12% were female and 10% were male. The mean BMI was 20.9 kg/m2 for female and 21.9 for kg/m2. Mild malnutrition, consequently low BMI has been demonstrated to be very common along with a poor mucosal recovery (Pulido *et al.,* 2013). Kabbani *et al.* (2012) also presented in their study with 679 patients changes in BMI post-diagnosis of CD. Normal BMI was verified in 65% of participants who were initially classified as underweight at diagnosis, and overweight or obese in 4.4%. A significant percentage remained underweight (30.4%). Majority of the patients (80.0%) with normal BMI at the diagnosis remained the same and a small group became overweight or obese (17.0%). By comparing those who increased (21.2%) their body weight to those who decrease (4.8%), they found a significant difference (p=0.0001). Amongst those who were overweight before treatment: 17.3%remained obese, 18.7% normal weight and a majority remained overweight (64%). Interestedly, they reported that patients who had good adherence and those with poor adherence to GFD did not differ in BMI. It is clear the existence of conflicting results between studies concerning to the protective effect of GFD (Norström et al., 2012). However, despite these conflicting results between studies analysed, it is important to note that overweight or obesity are considered one of the most important risk factors to diseases related to the heart (Rybak *et al.,* 2014; Kabbani *et al.,* 2012). Results a study demonstrated that patients who were on a GFD for 1 to 5 years had a significant increase in BMI (21.4 kg/m2 to 22.5 kg/m2; p<0.0001), as well as, total cholesterol (171.2 mg/dL to 181.4 mg/dL). On the other hand, a significant reduction in homocysteine (p=0.018) and triglycerides (p<0.0001). Thus proposing that patients diet were less probable to be artherogenic (Zanini *et al.,* 2013). None of the above studies related BMI with quality of patients GFD. However, This present study found a significant correlation between BMI and energy intake, fat and fibre. Nutritional status was reported to related to a series of factors, such as, level of malabsortion, persistent damage in the gastrointestinal tract, anxiety and depression, length of time that the patients has lived with untreated CD and nutritional adequacy of GFD (Niewinski, 2008; Häuser *et al.,* 2010). Therefore, alterations in BMI values may occur after alterations in the absorptive function of the intestinal

mucosa and in the patient diet and GFD introduction (Kabbani *et al.,* 2012; Kinsey *et al.,* 2008; Moreno *et al.,* 2014).

5.4. **Symptoms before and after GFD adherence**

Improvement in CD patients has been shown to occur in few weeks after gluten exclusion (Osman *et al.,* 2014). However, many patients can continue to experience clinical manifestations or symptoms related to CD while consume a GFD. This clinical event is characterized by several distinct diagnoses and it is known as non-responsive celiac (Leffler *et al.,* 2007; Maki, 2014). The most common reason for this clinical problem is the continued dietary exposure to food containing gluten or hypersensitivity to minimal amounts of gluten in foods considered as free from gluten (Jadresin *et al.,* 2008; Comino *et al.,* 2012; Ludvigsson *et al.,* 2014). This evidence is analogous to this study, as it was found presence of symptoms in 82.6% of the patients who are on a GFD, and both compliant and non-compliant patients reported these symptoms. The persistent symptoms most reported by compliant were nausea, vomiting and mouth ulcers, and most mentioned by noncompliant were fatigue, vomiting, nausea and diarrhoea. However, the number of compliant (59) patients who reported has not had any symptoms were very higher compared to non-compliant (13). Pulido *et al.,* (2013) who studied both symptom recovery and clinical features of 5912 adults coeliac patients found similar results. They showed that 80% of them admitted symptoms with a median duration of 24 hour, after introduction of a GFD. Furthermore, diarrhoea, abdominal pain, vomiting and bloating comprised the list of symptoms most reported. Similarly, results from a study by Murray *et al.* (2004) revealed that despite improvement of symptoms after GFD, 34% of 215 patients still had diarrhoea, 30% constipation, 9% vomiting or nausea and 3% abdominal pain. However, the gastrointestinal symptoms decreased significantly after compared to before GFD ($p<0.0001$). Nordstrom *et al.* (2012) following in the same line of research analysed symptoms pre-treatment and after, such as, flatulence, fatigue, soft stool, joint pain and abdominal pain. Pre-treatment and today most common symptoms were the same, flatulence and fatigue. The study also showed that despite the patients

reported persistent symptoms after GFD, there was an improvement of all symptoms reported, except joint pain, and a reduction in missed working days as well as in consumption of health care. Sainsbury *et al.* (2013) evaluated the severity of the persistent symptoms after GFD. Results showed that mild symptoms were mentioned by 15.9%, moderate by 28.2% and severe by 20.5% of the patients. Other study besides comparing symptoms before and after GFD, they also verified the difference between compliant and non-compliant in terms of clinical presentation and biochemical indicators, at 1-year of follow-up. No significant difference was found and poor compliance with GFD was highly associated to results of long-term impairment of quality of life (Nachman *et al.,* 2010). In another research Nachman *et al.* (2009) demonstrated that strictly compliant patients had significantly better quality of life, in terms of persistent symptoms, than moderate compliant patients ($p<0.0001$). Considering all these studies it is important to emphasize that persistent symptoms after dietary transgression do not affect all CD patients, and it may be important and helpful to the CD patients understand the importance of a strict GFD, and thus recognize the effect of gluten exposure, even a small quantity (Pulido *et al.,* 2013). In present study, majority of the patients reported symptoms for more than 3 years before being diagnosed with CD. Early age treatment of CD has been related to better compliance to GFD, and thus reduction of total illness burden and better quality of physical health in adulthood (Kurppa *et al.,* 2010; Schuppan and Zimmer, 2013). Although studies suggest that it is necessary greater effort to identify CD early and then initiate GFD introduction in order to reduce symptoms that are related to CD (Norström *et al.,* 2012), it has been reported that histological recovery of intestinal mucosa takes a certain period of time (Haines *et al.,* 2008).

5.5. **Implications and Limitations**

Findings of this study are in accordance with previous researches related to compliance with a GFD and nutritional adequacy of nutrients in CD patients, since it was shown a discrepancy between the level the compliance and malnutrition among patients. Therefore, results suggest a review of nutritional

recommendation for this group of population, as it is clear that they do not have the same clinical features as the general population. Moreover, the Codex standard should be stricter regarding the regulation of legislation that determines the presence of micronutrients in gluten free foods in a similar amount to the foods they are replacing.

Although it was used the best methods in order to collect dietary intake, they may be associated with bias due to their limitations. Since, omission of some foods (drinks and fillings) or meal as well as inaccurate evaluation of portions consumed can lead to underestimation of nutritional values ingested (Shepherd and Gibson, 2013; Halter *et al.,* 2002). Furthermore, Patients may be more cautious with their diet during the days of report, which may have influenced the nutritional adequacy outcomes in this research, as over-report was observed (Biagi *et al.,* 2009). Another limitation found was related to diet plan software. The program had lack of gluten free foods in their database, and thus, made difficult the process of nutrient analysis of this food group. However, even though the limitations had influenced the data, findings of this study are very satisfactory as it is consistent with some published studies (Butterworth et al., 2004; Biagi *et al.,* 2009).

5.6. **Future Research**

It is still much to be investigated regarding to GFD. One interesting point is to understand the mechanism and factors related to high level BMI in CD patients who are on a strict GFD. Studies have demonstrated that nutritional support and follow-up need to be improved, so, should be explored what difficulties are faced by the health professionals and identify possible interventions. Nutritional inadequacy has been indicated as one of the major cause of complications in CD, and there is few studies addressing this issue. This shows that greater attention should be given to this issue and further studies should be done.

6. CONCLUSION

In conclusion, despite this study has found high percentage of compliant patients, presence of nutritional deficiency and persistent symptoms were verified amongst those patients. This shows that all facets of the disease, not only gluten avoidance, should be should be analysed when is addressing about the treatment of celiac disease. As evidence has shown that the key aspects for the success of CD treatment, which includes a good compliance with a GED and a better quality of life, are medical support, the understanding the factors related to GFD adherence and find possible solutions and nutrition education.

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8. APPENDICES

8.1. APPENDIX 01: Compliance questionnaires.

University of Roehampton London

Questionnaires:

Instruction for filling the form: (Please read these carefully before you complete the form)

1. Please circle or tick the relevant option(s)
2. Where appropriate you may select more than one option
3. Please do not leave any question blank
4. If you do not know the answer, please write “don’t know” or “DK”
5. Please post the questionnaire back to us in the envelope provided.

Part A:

1. Sex Male Female

2. Age

18–30 31–40 41–50
51–60 more than 60

3. Which ethnic group do you belong too?

European Muslim Sikh Hindu

4. Are you a vegetarian?

Yes No

5. At what age were you diagnosed by the hospital to be suffering from coeliac disease?

18–30 31–40 41–50 51–60
more than 60

6. Did you have health problems in childhood?

Yes No

6. **What prompted you to consult your General Practitioner (GP)? [Please tick relevant option(s)]**
7.

Fatigue/ Hair loss Stomach pains/ bloating / Skin rash

Poor appetite/ Diarrhoea /Mouth ulceration Nausea/Vomiting

Weight loss /Family history Joint pains /Difficulty walking

8. How long had you been experiencing symptoms before you were diagnosed?

Less than 6 months 6 months to 1 year 1 year to 3 years more than 3 years

9. Did you know what coeliac disease was before you were diagnosed?

Yes No

10. At the time of your diagnosis, what was discussed at your consultation with your hospital doctor? [Please tick relevant option(s)]

Explained what coeliac disease was Told me to follow a strict gluten-free diet

Referred me to a dietician Arranged a follow-up appointment

Gave written information Other (please state)

11. Were you satisfied with the information given?

Yes No

12. If you were referred to a dietician, what advice were you given? [Please tick relevant option(s)]

Explained the diagnosis and the reasons for the dietARTICLE IN PRESS

Discussed a gluten-free diet

Discussed the Coeliac Society and local groups

Provided an information pack (containing diet sheet, food list, starter packs etc)

Discussed the prescribing of gluten-free products

A follow-up appointment was made

Given a contact telephone number for advice, if needed

13. Were you satisfied with the information given?

Yes No

If “No”, please state why:

14. Do you think the dietician should play an important role in the long-term management of Coeliac Disease?

Yes No

15. How often do you include gluten-containing foods in your diet?

Never Once a month Once a week Daily

Other please specify

16. What difficulties do you have in following a gluten-free diet? [Please tick relevant option(s)]

I don't understand what foods I can and cannot eat

I don't have the time to prepare different meals

Gluten-free foods have an unpleasant taste

Gluten-free foods are expensive to buy

My GP does not prescribe sufficient amounts of gluten-free products

I don't feel any different on a gluten-free diet

I don't understand the labelling on foods

17. Do you have symptoms when you eat food containing gluten?

Yes No

If yes, what symptoms do you experience? [Please tick relevant option(s)]

Nausea/vomiting Stomach pains Diarrhoea Fatigue/tiredness

Mouth ulcers Others (please specify)

18. Do you get gluten-free products on prescription?

Yes No

If No, did you know that they are available on prescription?

Yes No

If yes, do you get sufficient amounts of gluten-free products on prescription?

Yes No

19. Are you a member of the Coeliac Society?

Yes (please go to question 20) No

If you are not a member, is it because:- [please tick relevant option(s)]

You didn't know about it

You have a contact address, but haven't joined yet

You don't feel it is important

If I need advice, I will ask my GP

Other (please specify

Part B:

Please circle one option for each question in the columns from 1 to 5.

Questions	1	2	3	4	5
Have you been bothered by low energy level during the past 4 weeks?	None of the time	A little of the time	Some of the time	Most of the time	All of the time
Have you been bothered by headaches during the past 4 weeks?	None of the time	A little of the time	Some of the time	Most of the time	All of the time
I am able to follow a GFD when dining outside my home	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree
Before I do something I carefully consider the consequences	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree
I do not consider myself a failure	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree
How important to your health are accidental gluten exposures?	Very important	Somewhat important	Neutral/unsure	A little important	Not at all important
Over the past 4 weeks, how many times have you eaten foods containing gluten on purpose?	0-never	1-2	3-5	6-10	>10

Thank you for completing the questionnaire. Please use the enclosed stamped addressed envelope to return it to us.

Dr H Muhammad Questionnaire Version 1 30/06/2015

8.2. APPENDIX 02: Food diaries form example.

Food Diary
Please circle: Monday Tuesday Wednesday Thursday Friday Saturday Sunday

	Food	Amount (e.g., tbsp, can, serving)	Time	Where and Who with	Thoughts
Total number of 5 A Day portions			Have I reached my target?		

World Cancer Research Fund (WCRF UK) 22 Bedford Square, London WC1B 3HH Tel: 020 7343 4200 Web: www.wcrf-uk.org **Breakfast Mid 8.3.**

8.3. **APPENDIX 03: Ethical approval letters**

27 November 2014

Dr Humayun Muhammad University Hospital of Leicester Leicester General Hospital Gwendolen Rd, Leicester

LE5 4PW

Dear Dr Muhammad

Study title:

REC reference: Protocol number: IRAS project ID:

National Research Ethics Service

NRES Committee London - Queen Square

HRA NRES Centre Manchester Barlow House 3rd Floor 4 Minshull Street Manchester M1 3DZ

An investigation into dietary compliance of patients with coeliac disease 14/LO/2128 CD/RU/01

159160

The Proportionate Review Sub-committee of the NRES Committee London - Queen Square reviewed the above application on 20 November 2014.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager Rachel Heron, nrescommittee.london-queensquare@nhs.net.

Ethical opinion

On behalf of the Committee, the sub-committee gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified

below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

1. Please provide an explanation as to why the research will not be registered on a public database (Q50, page 14 of the IRAS form).

2. Participant Information A Research Ethics Committee established by the Health Research Authority

. a) Please make it explicit in both the Participant Information Sheet and Consent form that this research is being carried out as part of a PHD.

. b) On the Patient Information Sheet, the total approximate time required to complete the questionnaires should be reported: e.g. “Completing these questionnaires takes approximately 20 minutes in total”. This sentence could be added to the “What are the possible disadvantages and risks of taking part?” section.

. c) The Committee suggests adding the following sentence or similar to the section entitled ‘What are the possible disadvantages and risks of taking part’: “Some of the questions in the questionnaires may be of a sensitive nature. All information you give will be kept confidential. If you have any concerns, please do not hesitate to contact us."

. d) It should be clear on the patient information whether participants have to answer all the questions in the questionnaire, or whether they can omit some and still participate in the study.

Consent forms

a) The following sentence (“this information will always be anonymised”) should be added as shown here in capitals: “I understand that any information given by me may be used in future reports, articles or presentations by the research team. THIS INFORMATION WILL ALWAYS BE ANONYMISED. My General Practitioner GP may be contacted by the researcher.”

Invitation letter

a) For clarity, please add “(fifty pounds)” as shown here in capital letters: “There is a prize draw of £50.00 (FIFTY POUNDS) high street vouchers for participating in this study.”

Please also proof read material so that typos and minor errors are minimised.

You should notify the REC in writing once all conditions have been met

(except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated

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Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations. Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided

within IRAS.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see “Conditions of the favourable opinion”).

Summary of discussion at the meeting

Social or scientific value; scientific design and conduct of the study

The Committee queried why the research would not be registered on a public database.

Informed consent process and the adequacy and completeness of research participant information

The Committee felt that it should have been made clearer that information would be anonymised if used in future reports, articles or presentations.

The Committee noted a few minor points which needed to be clarified on the participant information sheets, which are listed above.

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Suitability of supporting information

The Commiittee noted that there was one area of clarification to be made on the invitation letter regarding payment.

Approved documents

The documents reviewed and approved were:

Document	Version	Date
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		12 August 2014
IRAS Checklist XML [Checklist_14112014]		14 November 2014
Letter from sponsor		21 October 2014
Letters of invitation to participant	2	01 October 2014
Other [CV S Reeves]		
Other [CV John Mayberry]		
Other [Permission from Dr Cooper to use questionnaire]		14 May 2014
Other [Permission from Dr Leffler to use questionnaire]		05 November 2014
Other [Food diary]		
Participant consent form	2	14 October 2014
Participant information sheet (PIS)	2	01 October 2014
REC Application Form [REC_Form_14112014]		14 November 2014
Research protocol or project proposal	2	01 October 2014
Summary CV for Chief Investigator (CI)		
Summary CV for supervisor (student research)		
Summary, synopsis or diagram (flowchart) of protocol in non technical language	2	01 October 2014
Validated questionnaire		30 June 2014

Membership of the Proportionate Review Sub-Committee

The members of the Sub-Committee who took part in the review are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document “After ethical review – guidance for researchers” gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol

A Research Ethics Committee established by the Health Research Authority

- Progress and safety reports
- Notifying the end of the study The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures. User Feedback The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/ HRA Training We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/ With the Committee’s best wishes for the success of this project. Yours sincerely On behalf of Gella Richards Vice Chair Email: nrescommittee.london-queensquare@nhs.net Enclosures: List of names and professions of members who took part in the review “After ethical review – guidance for researchers” [SL-AR2] Copy to: Mrs Jan Harrison Mrs Carolyn Maloney, University Hospitals of Leicester NHS Trust.
Dear Humayun,

Ethics Application

Applicant: **Humayun Muhammad**

Title: **An investigation into dietary compliance of patients with Coeliac Disease**

Reference: **LSC 14/ 112**

Department: **Life Sciences**

I have been advised that your above project has now received NHS REC approval (subject to conditions) - congratulations. Please note that it is your responsibility to meet any conditions imposed by the NHS in respect of this application. Please let us have the revised documentation in relation to the conditions imposed by them so that we can also confirm the amendments.

Condition:

Please advise us once NHS R&D approval have been received

Many thanks,

Jan

Jan Harrison Ethics Officer, Research Office, Department of Academic Enhancement University of Roehampton | London | SW15 5PJ

jan.harrison@roehampton.ac.uk| www.roehampton.ac.uk

Tel: +44 (0) 20 8392 5785

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8.3. **APPENDIX 04: Descriptive data.**

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Unique Patient ID	86	8	716	434.30	232.363
Gender	86	1	2	1.73	.445
what is the age of the patient	86	19	64	46.44	14.505
Which group do you belong to	86	0	4	1.06	.416
in Kgs	86	66.50	85.10	74.4523	4.42692
cm	86	157.00	177.00	164.9698	6.06116
Energyintake	86	636.00	2549.00	1390.2558	373.25784
BMI	86	22.60	31.50	27.4674	1.82166
Valid N (listwise)	86				

Which group do you belong to

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	1	1.2	1.2	1.2
	1	82	95.3	95.3	96.5
	2	1	1.2	1.2	97.7
	3	1	1.2	1.2	98.8
	4	1	1.2	1.2	100.0
	Total	86	100.0	100.0	

8.4. APPENDIX 05: Descriptive data by compliance groups.

Descriptive

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. Deviation
Gender	71	1	2	1.76	.430
what is the age of the patient	71	19	64	47.18	14.255
Which group do you belong to	71	0	4	1.03	.377
in Kgs	71	68.40	85.10	74.5620	4.34286
cm	71	157.00	177.00	164.5338	5.92947
Energyintake	71	727.00	2549.00	1400.4085	364.48827
Unique Patient ID	71	8	716	447.03	228.108
Valid N (listwise)	71				

a. Compliancegroup = Compliant

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. Deviation
Gender	15	1	2	1.60	.507
what is the age of the patient	15	21	64	42.93	15.664
Which group do you belong to	15	1	3	1.20	.561
in Kgs	15	66.50	83.50	73.9333	4.93293
cm	15	159.50	176.00	167.0333	6.45995
Energyintake	15	636.00	2355.00	1342.2000	422.63987
Unique Patient ID	15	56	710	374.07	250.874
Valid N (listwise)	15				

a. Compliancegroup = Non-cpmpliant

5.5. APPENDIX 06: Data of level compliance, percentage of GFD on prescription, and frequency of consumption of products containing gluten.

Statistics[a]

This is total leffler score, if above 19, the patient is strongly non-compliant

N	Valid	71
	Missing	0
Mean		12.0563
Std. Deviation		2.42539

a. Compliancegroup = Compliant

Statistics[a]

This is total leffler score, if above 19, the patient is strongly non-compliant

N	Valid	15
	Missing	0
Mean		20.1333
Std. Deviation		3.15926

a. Compliancegroup = Non cpmpliant

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
This is total leffler score, if above 19, the patient is strongly non-compliant	86	7.00	28.00	13.4651	3.99911
Valid N (listwise)	86				

Do you get gluten-free products on prescription?

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	30	34.9	34.9	34.9
	Yes	54	62.8	62.8	97.7
	2	2	2.3	2.3	100.0
	Total	86	100.0	100.0	

How often do you include gluten-containing foods in your diet?

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	3	3.5	3.5	3.5
	Never	60	69.8	69.8	73.3
	Once a month	13	15.1	15.1	88.4
	Once a week	3	3.5	3.5	91.9
	daily	5	5.8	5.8	97.7
	Other	2	2.3	2.3	100.0
	Total	86	100.0	100.0	

5.6. APPENDIX 07: Difference test for age, gender, ethnicity, weight, GFD on prescription and frequency of consumption of products containing gluten on diet between compliant and non-compliant

Frequencies:

How often do you include gluten containing foods in your diet?[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	3	4.2	4.2	4.2
	Never	52	73.2	73.2	77.5
	Once a month	9	12.7	12.7	90.1
	Once a week	2	2.8	2.8	93.0
	daily	3	4.2	4.2	97.2
	Other	2	2.8	2.8	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

Gender[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	17	23.9	23.9	23.9
	Female	54	76.1	76.1	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

Which group do you belong to[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	13	86.7	86.7	86.7
	2	1	6.7	6.7	93.3
	3	1	6.7	6.7	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

Do you get gluten-free products on prescription?[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	24	33.8	33.8	33.8
	Yes	45	63.4	63.4	97.2
	2	2	2.8	2.8	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

How often do you include gluten containing foods in your diet?[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Never	8	53.3	53.3	53.3
	Once a month	4	26.7	26.7	80.0
	Once a week	1	6.7	6.7	86.7
	daily	2	13.3	13.3	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

Gender[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	6	40.0	40.0	40.0
	Female	9	60.0	60.0	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

Which group do you belong to[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	13	86.7	86.7	86.7
	2	1	6.7	6.7	93.3
	3	1	6.7	6.7	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

Do you get gluten-free products on prescription?[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	40.0	40.0	40.0
	Yes	9	60.0	60.0	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

Mann-Whitney Test

Test Statistics[a]

	what is the age of the patient	in Kgs
Mann-Whitney U	464.500	486.500
Wilcoxon W	584.500	606.500
Z	-.775	-.524
Asymp. Sig. (2-tailed)	.439	.600

a. Grouping Variable: Compliancegroup

Statistics[a]

		what is the age of the patient	in Kgs
N	Valid	71	71
	Missing	0	0
Median		51.00	73.7000
Range		45	16.70

a. Compliancegroup = Compliant

Statistics[a]

		what is the age of the patient	in Kgs
N	Valid	15	15
	Missing	0	0
Median		42.00	72.7000
Range		43	17.00

a. Compliancegroup = Non-cpmpliant

8.5. APPENDIX 08: Dietary intake and meeting RNI-intake of micronutrients data

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Energyintake	86	636.00	2549.00	1390.2558	373.25784
Protein	86	22.70	115.10	51.2570	13.38587
Fat	86	20.10	114.40	54.1198	18.14885
Carbs	86	77.90	391.30	168.8198	55.53001
Fibre	86	5.30	31.70	14.5105	5.36483
VitaminB6	86	.31	2.60	1.1658	.40761
VintaminB12	86	.20	26.60	2.9605	2.98286
Folate	86	38.00	493.00	157.8488	76.89650
Iron	86	1.76	15.74	6.0466	2.87083
Calcium	86	103.00	2046.00	492.1977	257.62886
Fiberdensity	86	.44	2.30	1.0633	.35455
Valid N (listwise)	86				

FibermeetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1.00	4	4.7	4.7	4.7
	2.00	82	95.3	95.3	100.0
	Total	86	100.0	100.0	

VitaminB6meetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	30	34.9	34.9	34.9
	no	56	65.1	65.1	100.0
	Total	86	100.0	100.0	

VitamingB12meetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	58	67.4	67.4	67.4
	no	28	32.6	32.6	100.0
	Total	86	100.0	100.0	

FolatemeetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	1	1.2	1.2	1.2
	no	85	98.8	98.8	100.0
	Total	86	100.0	100.0	

IronmeetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	14	16.3	16.3	16.3
	no	72	83.7	83.7	100.0
	Total	86	100.0	100.0	

CalciummeetingRNI

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	3	3.5	3.5	3.5
	no	83	96.5	96.5	100.0
	Total	86	100.0	100.0	

APPENDIX 09: Difference test in nutrients intake between groups

Test Statistics[a]

	Energyintake	Protein	Fat	Carbs
Mann-Whitney U	469.000	410.000	459.500	508.500
Wilcoxon W	589.000	530.000	3015.500	628.500
Z	-.723	-1.394	-.831	-.273
Asymp. Sig. (2-tailed)	.470	.163	.406	.785

a. Grouping Variable: Compliancegroup

Test Statistics[a]

	Fibermeeting RNI	VitaminB6 meeting RNI	VitamingB12 meeting RNI	Fiberdensity
Mann-Whitney U	502.500	522.500	494.500	341.000
Wilcoxon W	3058.500	3078.500	614.500	461.000
Z	-.936	-.138	-.533	-2.180
Asymp. Sig. (2-tailed)	.349	.890	.594	.029

Test Statistics[a]

	Fibre	VitaminB6	VintaminB12	Folate	Iron	Calcium
Mann-Whitney U	376.500	504.000	469.000	476.500	449.000	381.500
Wilcoxon W	496.500	624.000	3025.000	596.500	3005.000	501.500
Z	-1.776	-.324	-.723	-.637	-.950	-1.718
Asymp. Sig. (2-tailed)	.076	.746	.470	.524	.342	.086

a. Grouping Variable: Compliancegroup

a. Grouping Variable: Compliancegroup

Test Statistics[a]

	Folatemeeting RNI	IronmeetingRNI	CalciummeetingRNI
Mann-Whitney U	525.000	465.500	510.000
Wilcoxon W	3081.000	585.500	3066.000
Z	-.460	-1.192	-.806
Asymp. Sig. (2-tailed)	.646	.233	.420

a. Grouping Variable: Compliancegroup

8.6. APPENDIX 10: APPENDIX 09: Difference in micronutrients meeting RNI-intake between groups.

FibermeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1.00	4	5.6	5.6	5.6
	2.00	67	94.4	94.4	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

VitamingB12meetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	47	66.2	66.2	66.2
	no	24	33.8	33.8	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

VitaminB6meetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	25	35.2	35.2	35.2
	no	46	64.8	64.8	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

FolatemeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	1	1.4	1.4	1.4
	no	70	98.6	98.6	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

CalciummeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	3	4.2	4.2	4.2
	no	68	95.8	95.8	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

IronmeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	10	14.1	14.1	14.1
	no	61	85.9	85.9	100.0
	Total	71	100.0	100.0	

a. Compliancegroup = Compliant

FibermeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2.00	15	100.0	100.0	100.0

a. Compliancegroup = Non-cpmpliant

VitaminB6meetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	5	33.3	33.3	33.3
	no	10	66.7	66.7	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

VitamingB12meetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	11	73.3	73.3	73.3
	no	4	26.7	26.7	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

FolatemeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	15	100.0	100.0	100.0

a. Compliancegroup = Non-cpmpliant

IronmeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	yes	4	26.7	26.7	26.7
	no	11	73.3	73.3	100.0
	Total	15	100.0	100.0	

a. Compliancegroup = Non-cpmpliant

CalciummeetingRNI[a]

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	no	15	100.0	100.0	100.0

a. Compliancegroup = Non-cpmpliant

8.7. **APPENDIX 11: Correlations analysis for BMI and fat, fibre and energy intake, data of mean BMI and differences in BMI between compliance groups.**

Correlations

			BMI	Fat	Fibre
Spearman's rho	BMI	Correlation Coefficient	1.000	.241*	.220*
		Sig. (2-tailed)	.	.026	.041
		N	86	86	86
	Fat	Correlation Coefficient	.241*	1.000	.288**
		Sig. (2-tailed)	.026	.	.007
		N	86	86	86
	Fibre	Correlation Coefficient	.220*	.288**	1.000
		Sig. (2-tailed)	.041	.007	.
		N	86	86	86

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Correlations

		Energyintake	BMI
Energyintake	Pearson Correlation	1	.304**
	Sig. (2-tailed)		.004
	N	86	86
BMI	Pearson Correlation	.304**	1
	Sig. (2-tailed)	.004	
	N	86	86

**. Correlation is significant at the 0.01 level (2-tailed).

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. Deviation
BMI	71	22.60	31.50	27.6535	1.80070
Valid N (listwise)	71				

a. Compliancegroup = Compliant

Descriptive Statistics[a]

	N	Minimum	Maximum	Mean	Std. Deviation
BMI	15	23.20	29.40	26.5867	1.71125
Valid N (listwise)	15				

a. Compliancegroup = Non-cpmpliant

Test Statistics[a]

	BMI
Mann-Whitney U	358.500
Wilcoxon W	478.500
Z	-1.981
Asymp. Sig. (2-tailed)	.048

a. Grouping Variable: Compliancegroup

8.8. APPENDIX 12: Data of symptoms before and after GFD.

Do you have symptoms when you eat food-containing gluten?

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	6	7.0	7.0	7.0
	Yes	71	82.6	82.6	89.5
	Not applicable	9	10.5	10.5	100.0
	Total	86	100.0	100.0	

Lenght_SymptomsBF

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	1	1.2	1.2	1.2
	Less than 6 months	11	12.8	12.8	14.0
	6 months to 1 year	16	18.6	18.6	32.6
	1 year to 3 years	25	29.1	29.1	61.6
	More than 3 years	31	36.0	36.0	97.7
	other	2	2.3	2.3	100.0
	Total	86	100.0	100.0	

8.9. APPENDIX 13: Data of types of symptoms mentioned

Crosstab

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD Nausea and vomitting	No	52	9	61
	Yes	19	6	25
Total		71	15	86

Crosstab

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD diarrhoea	No	36	9	45
	Yes	35	6	41
Total		71	15	86

Crosstab

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD fatigue	No	39	11	50
	Yes	32	4	36
Total		71	15	86

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD others	No	50	11	61
	Yes	21	4	25
Total		71	15	86

Crosstab

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD stomach pain	No	36	6	42
	Yes	35	9	44
Total		71	15	86

Crosstab

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD Not applibale because i dont eat GFD and hence dont know	no	59	13	72
	yes	12	2	14
Total		71	15	86

Count

		Compliancegroup		Total
		Compliant	Non-cpmpliant	
My symptom after ingestion of GFD mouth ulcers	No	63	13	76
	Yes	8	2	10
Total		71	15	86